Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Surveillance Summaries / Vol. 60 / No. 3
April 22, 2011

Malaria Surveillance — United States, 2009

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

CONTENTS

The *MMWR* series of publications is published by the Office of Surveillance, Epidemiology, and Laboratory Services, Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services, Atlanta, GA 30333.

Suggested Citation: Centers for Disease Control and Prevention. [Title]. MMWR 2011;60(No. SS-#):[inclusive page numbers].

Malaria Surveillance — United States, 2009

Sonja Mali, MPH
Kathrine R. Tan, MD, MPH
Paul M. Arguin, MD
Division of Parasitic Diseases and Malaria, Center for Global Health

Abstract

Problem/Condition: Malaria in humans is caused by intraerythrocytic protozoa of the genus *Plasmodium*. These parasites are transmitted by the bite of an infective female *Anopheles* mosquito. The majority of malaria infections in the United States occur among persons who have traveled to areas with ongoing malaria transmission. In the United States, cases can occur through exposure to infected blood products, congenital transmission, or local mosquitoborne transmission. Malaria surveillance is conducted to identify episodes of local transmission and to guide prevention recommendations for travelers.

Period Covered: This report summarizes cases in persons with onset of illness in 2009 and summarizes trends during previous years.

Description of System: Malaria cases diagnosed by blood film, polymerase chain reaction or rapid diagnostic tests are mandated to be reported to local and state health departments by health-care providers or laboratory staff. Case investigations are conducted by local and state health departments, and reports are transmitted to CDC through the National Malaria Surveillance System (NMSS), National Notifiable Diseases Surveillance System (NNDSS), or direct CDC consults. Data from these reporting systems serve as the basis for this report.

Results: CDC received reports of 1,484 cases of malaria, including two transfusion-related cases, three possible congenital cases, one transplant case and four fatal cases, with an onset of symptoms in 2009 among persons in the United States. This number represents an increase of 14% from the 1,298 cases reported for 2008. *Plasmodium falciparum*, *P. vivax*, *P. malariae*, and *P. ovale* were identified in 46%, 11%, 2%, and 2% of cases, respectively. Thirteen patients were infected by two or more species. The infecting species was unreported or undetermined in 38% of cases. Among the 1,484 cases 1,478 were classified as imported. Among the 103 U.S. civilians for whom information on chemoprophylaxis use and travel area was known, only 34 (33%) reported that they had followed and adhered to a chemoprophylactic drug regimen recommended by CDC for the area to which they had traveled. Nineteen cases were reported in pregnant women, among whom none adhered to chemoprophylaxis. Almost 22% of the cases among pregnant women were treated with an inappropriate treatment drug regimen, of which 39% were among cases with either a *P. vivax* or *P. ovale* infection where primaquine was not taken. Among all the reasons for travel, travelers visiting friends and relatives (VFR) and missionaries were the groups with the lowest proportion of chemoprophylexis use.

Interpretation: A notable increase in the number of malaria cases was reported from 2008 to 2009; however, the number of cases in 2009 is consistent with the average number of cases reported during the preceding 4 years. In the majority of reported cases, U.S. civilians who acquired infection abroad had not adhered to a chemoprophylaxis regimen that was appropriate for the country in which they acquired malaria. Furthermore, treatment of malaria, while appropriate for the majority of cases, was insufficient for a large number of *P. vivax* and *P. ovale* infections, putting patients at risk for relapsing malaria.

Public Health Actions: Decreasing the number of malaria cases in subsequent years will require conveying the importance of adhering to appropriate preventive measures for malaria specifically targeting travelers visiting friends and relatives, missionary, and pregnant populations. Clinicians require education on the need to encourage use of malaria prophylaxis and need further information on the appropriate diagnostic and treatment guidelines for malaria. Malaria prevention recommendations are available online (http://www.cdc.gov/malaria/travelers/ or http://wwwnc.cdc.gov/travel/yellowbook/2010/chapter-2/malaria.aspx#990). Malaria infections can be fatal if not diagnosed and treated promptly with antimalarial medications appropriate for the individual patient's age and medical history, the likely site of malaria acquisition, and previous use of antimalarial chemoprophylaxis. Clinicians should consult the CDC Guidelines for Treatment and contact the CDC's Malaria Hotline for case management advisement when needed. Malaria treatment recommendations can be obtained online (http://www.cdc.gov/malaria/diagnosis_treatment) or by calling the Malaria Hotline (770-488-7788).

Corresponding author: Sonja Mali, MPH, Division of Parasitic Diseases, Center for Global Health, 4770 Buford Hwy., N.E., MS F-22, Atlanta, GA 30341. Telephone: 770-488-7757; Fax: 770-488-4465; E-mail: smali@cdc.gov.

Introduction

Malaria in humans is caused by infection with one or more of several species of *Plasmodium* (i.e., *P. falciparum*, *P. vivax*, *P. ovale*, *P. malariae* and occasionally other *Plasmodium* species). The infection is transmitted by the bite of an infective female *Anopheles* sp. mosquito. *P. falciparum* and *P. vivax* species cause the most infections worldwide. *P. falciparum* is the agent that most commonly causes severe and potentially fatal malaria. Globally, an estimated 243 million clinical cases and 863,000 deaths were reported in 2008, mostly in children aged <5 years living in sub-Saharan Africa (*1*). *P. vivax* and *P. ovale* have dormant liver stages, which can reactivate and cause malaria several months or years after the bite of an infected mosquito. *P. malariae* can result in long-lasting infections and if untreated can persist asymptomatically in the human host for years, even a lifetime (*1*). *P. knowlesi*, a parasite of Asian macaques, has been documented as a cause of human infections and some fatalities in Southeast Asia. Investigations are ongoing to determine the extent of its transmission to humans (*2*). Approximately half of the world's population live in areas where malaria is transmitted (i.e., approximately 100 countries in parts of Africa, Asia, the Middle East, Eastern Europe, Central and South America, Caribbean, and Oceania). Before the 1950s, malaria was endemic throughout the southeastern United States; an estimated 600,000 cases occurred in 1914 (*3*). During the late 1940s, a combination of improved housing and socioeconomic conditions, environmental management, vector-control efforts, and case management was successful at interrupting malaria transmission in the United States. Since then, malaria case surveillance has been maintained to detect locally acquired cases that could indicate the reintroduction of transmission and to monitor patterns of resistance to antimalarial drugs. Malaria vector mosquitoes are still present in the United States.

The majority of reported malaria cases diagnosed each year in the United States are imported from regions where malaria transmission is known to occur, although congenital infections and infections resulting from exposure to blood or blood products also are reported in the United States. In addition, occasionally, a limited number of cases are reported that might have been acquired through local mosquito borne transmission (*4*).

State and local health departments and CDC investigate malaria cases acquired in the United States, and CDC analyzes data from imported cases to detect trends in acquisition. This information is used to guide malaria prevention recommendations for international travelers.

The signs and symptoms of malaria illness are varied, but the majority of patients have fever. Other common symptoms include headache, back pain, chills, increased sweating, myalgia, nausea, vomiting, diarrhea, and cough. The diagnosis of malaria should always be considered for persons with these symptoms who have traveled to an area with known malaria transmission. Malaria also should be considered in the differential diagnosis of persons who have fever of unknown origin, regardless of their travel history. Untreated infections can rapidly progress to coma, renal failure, respiratory distress, and death. This report summarizes malaria cases reported to CDC among persons with onset of symptoms in 2009.

Methods

Data Sources

Malaria case data are reported to the National Malaria Surveillance System (NMSS) and the National Notifiable Diseases Surveillance System (NNDSS) (*5*). Although both systems rely on passive reporting, the numbers of reported cases might differ because of differences in collection and transmission of data. A substantial difference between the data collected in these two systems is that NMSS receives more detailed clinical and epidemiologic data regarding each case (e.g., information concerning the area to which the infected person has traveled). Malaria cases can be reported to CDC through either the NMSS, NNDSS, or through a direct consultation with CDC Malaria staff; therefore cases captured through these various paths are compared, de-duplicated, compiled, and analyzed. This report presents data on the aggregate of cases reported to CDC through all reporting systems.

Blood-film–confirmed, Polymerase chain reaction(PCR)-confirmed, or RDT diagnostic tested (RDT) malaria cases among civilians and military personnel are identified by health-care providers or laboratories. Each confirmed malaria case is reported to local or state health departments and to CDC. CDC staff review all reports when received and request additional information from the provider or the state, if necessary (e.g., when no recent travel to a malarious country is reported). Reports of other cases are telephoned to CDC directly by health-care providers, usually when they are seeking assistance with diagnosis or treatment. Information regarding cases reported directly to CDC is shared with the relevant state health department. All possible cases that have been reported as acquired in the United States are investigated further, including all induced, congenital, introduced, and cryptic cases (see "Definitions"). Information derived from uniform case report forms is entered into a database and analyzed annually.

An estimated case rate for each country was calculated using estimates of travel volume for U.S. travelers to each country where cases of malaria were acquired and the number of cases

among U.S. travelers attributable to each country. Data used to estimate country-specific relative case rates were extrapolated from World Tourism Organization estimates of annual numbers of U.S. travelers to specified countries (*6*). Estimated relative case rates were determined by dividing the individual country-specific case rates by the median individual country-specific case rate. The chi-square test was used to calculate p values and assess differences between variables reported in 2008 compared with previous years. A p value of <0.05 was considered statistically significant.

Definitions

The following definitions are used in malaria surveillance for the United States:

- **U.S. resident** – Any person residing in the United States including both civilians and U.S. military personnel regardless of legal citizenship**.**
- **U.S. civilian** – U.S. residents, excluding U.S. military personnel.
- **Foreign resident** – Persons who hold resident status in a country other than the United States.
- **Traveler visiting friends or relatives** – An immigrant, ethnically and racially distinct from the major population of the country of residence (a country where malaria is not endemic), who returns to his/her homeland (a country where malaria is endemic) to visit friends or relatives. Included in the VFR category are family members (e.g., spouse or children) who were born in the country of residence.
- **Laboratory criteria for diagnosis:** Demonstration of malaria parasites on blood film, PCR or by RDT (followed by blood film confirmation).
- **Confirmed case:** Symptomatic or asymptomatic infection that occurs in a person in the United States or one of its territories who has laboratory-confirmed (by microscopy or PCR) malaria parasitemia, regardless of whether the person had previous episodes of malaria while in other countries. A subsequent episode of malaria is counted as an additional case, regardless of indicated *Plasmodium* species, unless the case is indicated as a treatment failure resulting from drug resistance. This report also uses terminology derived from the recommendations of the World Health Organization (*6*). Definitions of the following terms are included for reference:
- **Autochthonous malaria:**
  - **Indigenous.** Mosquitoborne transmission of malaria in a geographic area where malaria occurs regularly.
  - **Introduced.** Mosquitoborne transmission of malaria from a person with an imported case in an area where malaria does not occur regularly.
- **Imported malaria:** Malaria acquired outside a specific area. In this report, imported cases are those acquired outside the United States and its territories.
- **Induced malaria:** Malaria acquired through artificial means (e.g., blood transfusion, organ transplantation or by using shared syringes).
- **Relapsing malaria:** Recurrence of disease after it has been apparently cured. In malaria, true relapses are caused by reactivation of dormant liver stage parasites (hypnozoites) of *P. vivax* and *P. ovale*.
- **Severe malaria:** a case of malaria with one or more of the following manifestations: neurologic symptoms, renal failure, severe anemia (defined by hemoglobin [Hb] <7g/dL), acute respiratory distress syndrome (ARDS), jaundice, or ≥5% parasitemia (7). In the attempt to capture severe cases where clinical criteria were not reported, persons who were treated for severe malaria (i.e., artesunate, quinidine, and/or an exchange blood transfusion) despite having no specific severe manifestations reported also will be counted as a severe case in this analysis.
- **Cryptic malaria:** A case of malaria for which epidemiologic investigations fail to identify a plausible mode of acquisition (this term applies primarily to cases found in countries where malaria is not endemic).

Laboratory Diagnosis of Malaria

To diagnose malaria early and promptly, physicians must obtain a travel history from every febrile patient. Malaria should be included in the differential diagnosis of every febrile patient who has traveled to a malarious area. If malaria is suspected, a Giemsa-stained film of the patient's peripheral blood should be examined for parasites as soon as possible. Thick and thin blood films must be prepared correctly because diagnostic accuracy depends on blood-film quality and examination by experienced laboratory personnel (*8*). Some reference laboratories and health departments can diagnose malaria using PCR, although this is generally reserved for cases for which blood-film diagnosis of malaria is inadequate and for confirmation of species. PCR results are also often not available quickly enough to be of use in the initial diagnosis of a patient with malaria.

In addition, BinaxNOW Malaria, an RDT that detects circulating malaria-specific antigens, is widely available for use by U.S. laboratories. The test is only approved for use by hospital and commercial laboratories, not by individual clinicians or the general public (*8*). In the United States, use of RDTs can decrease the amount of time required to determine whether

a patient is infected with malaria but does not eliminate the need for standard tests (*9*). Positive and negative RDTs must be confirmed by microscopy. RDTs are not able to speciate or quantitate malaria parasites (*10*).

Results

General Surveillance

In 2009, CDC received 1,484 reports concerning cases of malaria among persons in the United States and its territories, representing a 14% increase from the 1,298 cases reported with onset in 2008 (*8*). In 2009, a total of 679 cases occurred among U.S. residents, 201 cases among foreign residents, and 604 cases among patients with unknown or unreported resident status (Table 1). Among cases in patients with known resident status, no significant changed occurred between 2008 and 2009 in the proportion of cases among military and foreign residents. However, there was a significant difference in the proportion of cases among U.S residents and patients with unknown resident status (between 2008 and 2009, an increase of 30% and 2%, respectively, in 2009.

Plasmodium Species

Among the 1,484 cases reported in 2009, the infecting species of *Plasmodium* was identified and reported in 927 (63%) cases (Table 2). *P. falciparum* and *P. vivax* comprised the majority of infections and were identified in 74% and 18% of infected persons with species reported, respectively. Among 894 cases for which both the region of acquisition and the infecting species were known, *P. falciparum* accounted for 88% of infections acquired in Africa, 73% in the Americas, 12% in Asia, and 14% in Oceania. Infections attributed to *P. vivax* accounted for 4% acquired in Africa, 24% in the Americas, 78% in Asia, and 86% in Oceania.

Region of Acquisition and Diagnosis

Among the 1,484 reported cases, 1,478 were classified as imported cases; three congenital cases and three transplant/transfusion cases were not counted as imported cases. Of 987 imported cases for which the region of acquisition was known, 735 (74%) were acquired in Africa, 142 (14%) in Asia, 103 (10%) in the Americas, and 7 (1%) in Oceania. West Africa accounted for 595 (81%) cases acquired in Africa. In Asia, 199 (85%) cases were acquired in South Asia, of which 92 (46%) were acquired in India. Eighteen cases (17%) were acquired in Central America, of which the majority (n = 12 [67%]) was from Honduras. The Caribbean region accounted for 61% (n = 63) of the cases in the Americas, of which 56% (n = 58) were from Haiti. Twenty-two (21%) cases were acquired in South America, of which 59% (n = 13) were from Guyana. Information regarding region of acquisition was missing for 491 (33%) imported cases (Table 3).

In the United States, seven jurisdictions accounted for approximately 50% of the reported cases: New York City (n = 209), California (n = 126), New Jersey (n=103), Florida (n = 94), Texas (n = 87), Maryland (n = 80), and Georgia (n = 74) (Figure). The states with the most significant change in reported malaria burden in 2009 were Florida, Indiana, New Jersey, and Wisconsin. The number of cases reported in Florida increased from 58 cases in 2008 to 94 cases in 2009. Cases in Indiana increased by 19 cases, from the six cases reported in 2008. In addition, the number of cases in New Jersey increased by 63%, and the number of cases in Wisconsin decreased by 52% from 2008.

Imported Malaria by Resident Status

Among the 875 imported malaria cases of known resident status, 677 (77%) occurred among U.S. residents and 198 (23%) among residents of other countries. Among the 677 imported malaria cases among U.S. residents, 509 (75%) were acquired in Africa, 81 (12%) were acquired in the Americas, and 75 (11%) were acquired in Asia (Table 4). Of the 198 imported cases among foreign residents, 132 (67%) were acquired in Africa and 49 (25%) were acquired in Asia. Among those foreign cases in persons for whom purpose of visit was known, 89 (45%) occurred in recent immigrants or refugees, and 46 (23%) occurred in persons who were visiting friends and relatives in the United States.

Interval Between Arrival in the United States and Illness Onset

Among the 1,478 imported malaria cases, the interval between both the date of arrival in the United States and onset of illness and the infecting *Plasmodium* species were known for 638 (43%) cases. Symptoms began before arrival in the United States for 103 (16%) patients and on or after arrival for 535 (84%) patients. Onset of malaria symptoms occurred <1 month after arrival in 395 (81%) of the 489 *P. falciparum* patients and in 55 (56%) of the 98 *P. vivax* patients (Table 5).

Imported Malaria Among U.S. Military Personnel

In 2009, a total of 18 cases of imported malaria were reported among U.S. military personnel. Nine persons reported travel to Africa, and six reported travel to Afghanistan. One reported travel to the Middle East region, and region of travel

TABLE 1. Number of malaria cases* among U.S. military personnel, U.S. civilians, and foreign civilians — United States, 1977–2009

Year	U.S. military personnel	U.S. civilians	Foreign civilians	Status not recorded†	Total
1977	11	233	237	0	**481**
1978	31	270	315	0	**616**
1979	11	229	634	3	**877**
1980	26	303	1,534	1	**1,864**
1981	21	273	809	0	**1,103**
1982	8	348	574	0	**930**
1983	10	325	468	0	**803**
1984	24	360	632	0	**1,016**
1985	31	446	568	0	**1,045**
1986	35	410	646	0	**1,091**
1987	23	421	488	0	**932**
1988	33	550	440	0	**1,023**
1989	35	591	476	0	**1,102**
1990	36	558	504	0	**1,098**
1991	22	585	439	0	**1,046**
1992	29	394	481	6	**910**
1993	278	519	453	25	**1,275**
1994	38	524	370	82	**1,014**
1995	12	599	461	95	**1,167**
1996	32	618	636	106	**1,392**
1997	28	698	592	226	**1,544**
1998	22	636	361	208	**1,227**
1999	55	833	381	271	**1,540**
2000	46	827	354	175	**1,402**
2001	18	891	316	158	**1,383**
2002	33	849	272	183	**1,337**
2003	36	767	306	169	**1,278**
2004	32	775	282	235	**1,324**
2005	36	870	297	325	**1,528**
2006	50	736	217	561	**1,564**
2007	33	701	263	508	**1,505**
2008	19	510	176	593	**1,298**
2009	18	661	201	604	**1,484**

* A case was defined as symptomatic or asymptomatic illness that occurs in the United States or one of its territories in a person who has laboratory-confirmed malaria parasitemia (by microscopy or polymerase chain reaction), regardless of whether the person had previous attacks of malaria while in other countries. A subsequent attack of malaria occurring in a person is counted as an additional case if the demonstrated *Plasmodium* species differs from the initially identified species or if it is indicated as a relapsing infection demonstrating *Plasmodium* species is the same species identified previously. If a subsequent attack of malaria occurs as a result of treatment failure then the case is not counted as an additional case.

† The increase in persons with unknown civil status that began in the 1990s might be attributed to a change in the surveillance form.

was unspecified in two persons. Information on infecting species was known for 14 cases; six cases were identified as *P. falciparum,* six cases as *P. vivax,* one case as *P. malariae,* and one case was reported as a mixed infection of *P. falciparum* and *P. malariae.* Among those 18 cases, 14 occurred in persons who reported having taken an appropriate drug for primary chemoprophylaxis. However, among the six patients infected with *P. vivax*, none reported taking primaquine for presumptive antirelapse therapy, which also was indicated in these instances. Of all imported cases, only five patients reported adherence (no missed doses) to the prescribed drug regimen. These cases were reported by state health departments and do not include all cases that might have occurred among all military personnel.

Chemoprophylaxis Use Among U.S. Civilians

Information about chemoprophylaxis use and travel area was known for 611 (93%) of the 659* U.S. civilians who had imported malaria. Of these 611 persons, 155 (25%) had taken chemoprophylaxis, a percentage that has been decreasing since 2005. Among the 155 persons who reported taking malaria chemoprophylaxis, 15 (10%) had not taken a medication recommended by CDC for the area visited and 103 (66%) had taken a CDC-recommended medication. The specific drug taken, if any, was not reported for the remaining 37 (24%) travelers. Of the 103 who reported taking CDC-recommended chemoprophylaxis, 37 (36%) had taken mefloquine, 38 (37%) had taken doxycycline, 18 (18%) had taken atovaquone/proguanil, two (2%) had taken primaquine, and six (6%) had taken chloroquine. Two additional patients had taken a combination of two CDC-recommended malaria chemoprophylactics for the specific travel region. Information about infecting species was available for 93 (90%) patients who had

* A congenital and transfusion case was excluded from the total number of imported U.S. civilian cases.

TABLE 2. Number and percentage of malaria cases, by Plasmodium species — United States, 2007–2009

	2007		2008		2009	
***Plasmodium* species**	**No.**	**(%)**	**No.**	**(%)**	**No.**	**(%)**
P. falciparum	654	(43.4)	527	(40.6)	687	(46.3)
P. vivax	305	(20.3)	190	(14.6)	166	(11.2)
P. malariae	30	(2.0)	19	(1.5)	32	(2.1)
P. ovale	53	(3.5)	18	(1.4)	29	(2.0)
P. knowlesi	0	(0)	1	(0.1)	0	(0)
Mixed	9	(0.6)	8	(0.6)	13	(0.9)
Undetermined	454	(30.2)	535	(41.2)	557	(37.5)
Total	1,505	(100)	1,298	(100)	1,484	(100)

TABLE 3. Number of imported malaria cases, by country of acquisition and Plasmodium species — United States, 2009

Country of acquisition	*P. falciparum*	*P. vivax*	*P. malariae*	*P. ovale*	Unknown	Mixed	Total
Africa	**579**	**23**	**22**	**23**	**77**	**11**	**735**
Angola	2	0	0	0	0	0	**2**
Benin	5	0	0	0	1	0	**6**
Burkina Faso	9	0	0	0	0	0	**9**
Burundi	0	1	0	0	0	0	**1**
Cameroon	12	0	1	1	5	1	**20**
Central African Republic	1	0	0	0	0	0	**1**
Chad	1	0	0	0	0	0	**1**
Congo, Democratic Republic of	2	0	0	0	0	0	**2**
Congo, Republic of	5	0	0	2	0	1	**8**
Côte d'Ivoire	30	0	1	1	0	0	**32**
Equatorial Guinea	1	0	0	1	0	0	**2**
Ethiopia	3	13	1	0	0	0	**17**
Gambia	2	0	0	0	0	0	**2**
Ghana	86	1	3	6	3	0	**99**
Guinea	17	0	0	1	5	2	**25**
Kenya	6	0	2	1	5	1	**15**
Liberia	17	0	0	1	6	0	**24**
Malawi	9	0	0	0	0	0	**9**
Mali	8	0	1	0	4	0	**13**
Mozambique	2	0	0	0	0	1	**3**
Nigeria	214	3	5	5	25	2	**254**
Rwanda	1	1	0	0	1	0	**3**
Senegal	10	0	0	0	0	0	**10**
Sierra Leone	41	0	2	0	6	0	**49**
Somalia	1	0	0	0	0	0	**1**
South Africa	1	0	0	0	1	0	**2**
Sudan	9	1	0	0	2	0	**12**
Tanzania	1	0	0	0	1	0	**2**
Togo	8	0	1	0	2	0	**11**
Uganda	18	1	3	1	1	1	**25**
Zambia	2	0	0	0	0	0	**2**
Zimbabwe	1	0	0	0	0	0	**1**
West Africa, unspecified	19	0	1	1	2	0	**23**
East Africa, unspecified	9	2	0	0	0	1	**12**
Southern Africa, unspecified	1	0	0	0	0	0	**1**
Africa, unspecified	25	0	1	2	7	1	**36**
Asia	**13**	**106**	**6**	**6**	**10**	**1**	**142**
Afghanistan	0	6	0	1	1	0	**8**
Burma (Myanmar)	0	2	0	0	0	0	**2**
India	7	72	4	2	6	1	**92**
Indonesia	2	0	0	0	1	0	**3**
Pakistan	0	13	2	1	1	0	**17**
Philippines	0	2	0	0	0	0	**2**
Saudi Arabia	1	0	0	0	0	0	**1**
Thailand	2	8	0	1	1	0	**12**
Asia, Southeast	0	1	0	0	0	0	**1**
Asia, unspecified	1	1	0	1	0	0	**3**
Middle East	0	1	0	0	0	0	**1**

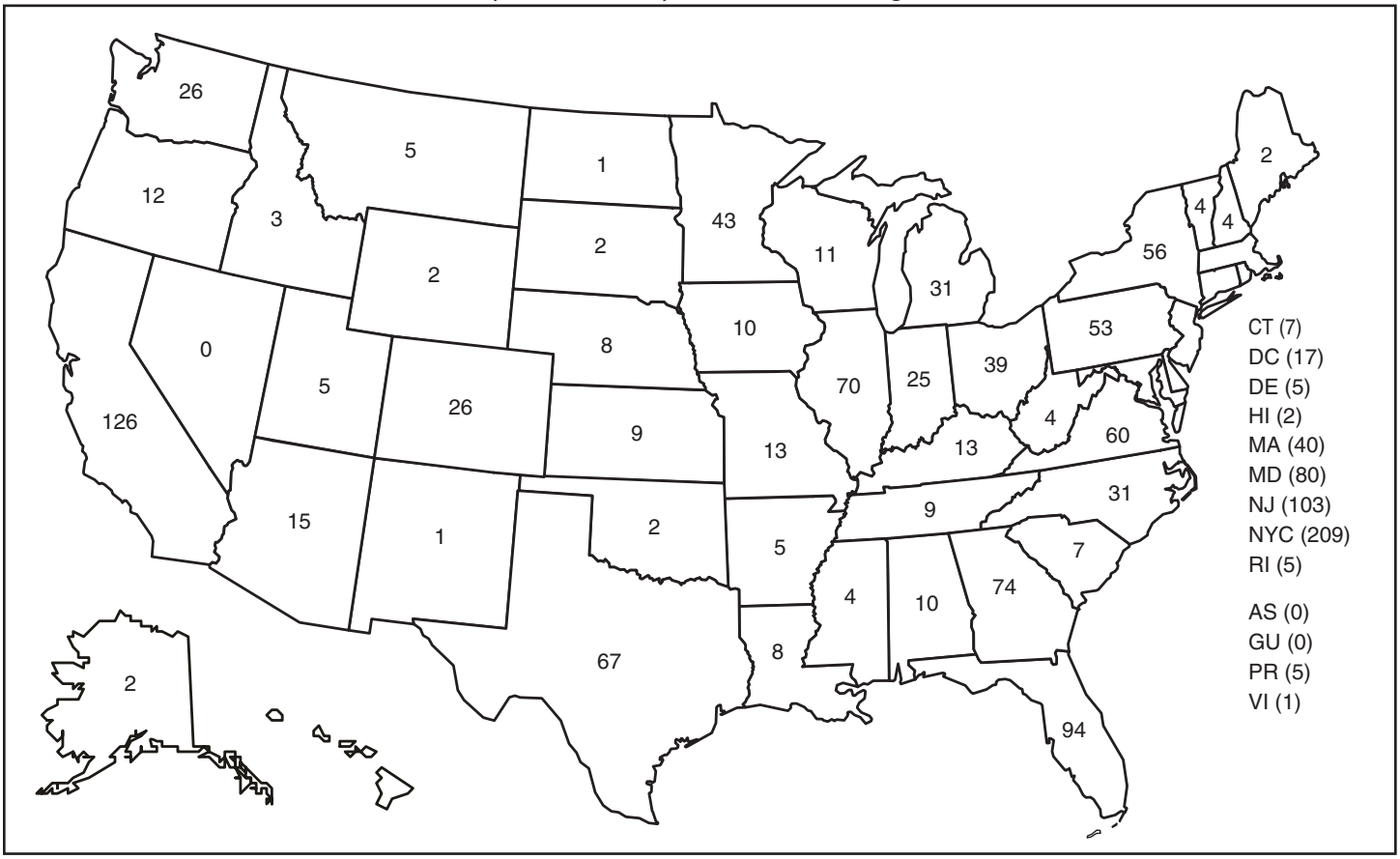
taken a recommended antimalarial drug and was undetermined for the remaining 10 patients. Moreover, among the 91 who reported taking CDC-recommended chemoprophylaxis and for whom adherence was known, most (n=57 [55%]) reported nonadherence (missed doses). Although adherence with an appropriate drug regimen for prevention in 2009 appears to have improved slightly since 2008, drug adherence has been trending downward since 2005.

Cases of P. vivax *or* P. ovale *After Recommended Prophylaxis Use.* Among the 93 patients who took chemoprophylaxis appropriately and had information on infecting species, 13 (14%) cases were caused by *P. vivax*, and four (4%) cases were caused by *P. ovale*. Of the 17 cases of *P. vivax* or *P. ovale*, information on five cases was insufficient (i.e., missing data regarding symptom onset or return date from travel) to assess a relapse infection due to missing data regarding symptom onset or return date. Six cases occurred >45 days after the patient's arrival in the United States. These cases were consistent with relapsing infections and do not indicate primary prophylaxis failures. Six cases occurred ≤45 days after the patient returned to the United States. Two of the six patients were nonadherent with their malaria chemoprophylaxis regimen. The four

TABLE 3. (*Continued*) Number of imported malaria cases, by country of acquisition and Plasmodium species — United States, 2009

Country of acquisition	*P. falciparum*	*P. vivax*	*P. malariae*	*P. ovale*	Unknown	Mixed	Total
Central America and the Caribbean	**62**	**12**	**2**	**0**	**5**	**0**	**81**
Dominican Republic	4	0	0	0	0	0	**4**
Guatemala	1	1	1	0	0	0	**3**
Haiti	57	0	0	0	1	0	**58**
Honduras	0	8	0	0	4	0	**12**
Mexico	0	2	0	0	0	0	**2**
Nicaragua	0	1	0	0	0	0	**1**
Caribbean, unspecified	0	0	1	0	0	0	**1**
South America	**10**	**8**	**0**	**0**	**3**	**1**	**22**
Brazil	0	4	0	0	0	0	**4**
Colombia	3	0	0	0	0	0	**3**
French Guiana	0	0	0	0	1	0	**1**
Guyana	7	3	0	0	2	1	**13**
Peru	0	1	0	0	0	0	**1**
Oceania	**1**	**6**	**0**	**0**	**0**	**0**	**7**
Papua New Guinea	1	5	0	0	0	0	**6**
Solomon Islands	0	1	0	0	0	0	**1**
Unknown	19	9	2	0	461	0	**491**
Total	**684**	**164**	**32**	**29**	**556**	**13**	**1478**

FIGURE 1. Number of malaria cases (N = 1,484), by state or territory in which case was diagnosed — United States, 2009



Abbreviations: AS = American Samoa; GU = Guam; PR = Puerto Rico; VI = U.S. Virgin Islands.

TABLE 4. Number and percentage of imported malaria cases among U.S. and foreign residents, by region of acquisition — United States, 2009*

	United States		Foreign		Total	
Area or region	**No.**	**(%)**	**No.**	**(%)**	**No.**	**(%)**
Africa	509	(75.2)	132	(66.7)	**641**	**(73.3)**
Asia	75	(11.1)	49	(24.7)	**124**	**(14.2)**
Central America/Caribbean	64	(9.4)	10	(5.0)	**74**	**(8.4)**
South America	17	(2.5)	4	(2.0)	**21**	**(2.4)**
Oceania	7	(1.0)	0	(0)	**7**	**(0.8)**
Unknown	5	(0.7)	3	(1.5)	**8**	**(0.9)**
Total	**677**	**(100)**	**198**	**(100)**	**875**	**(100)**

* Persons for whom U.S. or foreign status was not known were excluded.

TABLE 5. Number and percentage of imported malaria cases, by interval between date of arrival in the United States and onset of illness and by *Plasmodium* species* — United States, 2009

	P. falciparum		*P. vivax*		*P. malariae*		*P. ovale*		Mixed		Total	
Interval (days)	**No.**	**(%)**	**No.**	**(%)**	**No.**	**(%)**	**No**	**(%)**	**No**	**(%)**	**No.**	**(%)**
< 0†	72	(14.7)	19	(19.4)	5	(23.8)	4	(19.0)	3	(33.3)	**68**	**(12.9)**
0–29	395	(80.8)	55	(56.1)	9	(42.8)	9	(42.8)	5	(55.6)	**393**	**(74.5)**
30–89	16	(3.3)	13	(13.2)	5	(23.8)	3	(14.3)	0	(0)	**31**	**(5.9)**
90–179	1	(0.2)	8	(8.2)	1	(4.8)	4	(19.0)	0	(0)	**22**	**(4.2)**
180–364	5	(1.0)	3	(3.1)	1	(4.8)	1	(4.8)	1	(11.1)	**12**	**(2.3)**
>365	0	(0)	0	(0)	0	(0)	0	(0)	0	(0)	**1**	**(0.2)**
Total	**489**	**(100)**	**98**	**(100)**	**21**	**(100)**	**21**	**(100)**	**9**	**(100)**	**527**	**(100)**

* Persons for whom *Plasmodium* species, date of arrival in the United States, or date of onset of illness is unknown are not included.
† Persons with an interval of <0 days had onset of illness before arriving in the United States.

patients who reported adherence with an antimalarial chemoprophylaxis regimen had traveled to Africa and had all taken atovaquone/proguanil for malaria chemoprophylaxis. Possible explanations for these cases include inappropriate dosing, unreported nonadherence, malabsorption of the drug, an early relapse from hypnozoites established at the start of this trip, or possibly emerging parasite resistance.

Cases of P. falciparum *or* P. malariae *After Recommended Prophylaxis Use.* The 76 cases of malaria reported among persons who had taken a recommended antimalarial drug for chemoprophylaxis included 73 cases of *P. falciparum* and three cases of *P. malariae.* Of the 73 *P. falciparum* cases, 71 (94%) were acquired in Africa and two cases were acquired in Haiti. Forty-six (63%) of the 73 *P. falciparum* patients reported nonadherence to the antimalarial drug regimen and 10 cases had no adherence information available. In 17 (23%) cases, patients reported adherence with antimalarial chemoprophylaxis, of which 13 (76%) had traveled to Africa. Of the three *P. malariae* cases, two were acquired in Africa and one in India. Of the three cases, two reported adherence to the antimalarial drug regimen.

Patients with History of Malaria

Of the 1,478 imported cases, data on history of malaria was known for 830 (56%) cases; 118 (14%) patients specified having history of a malaria infection during the preceding 12 months. Among the 118 cases, 33 (28%) were caused by *P. vivax* and four (3%) by *P. ovale.* A total of 17 probable relapses (see definition of *Relapsing malaria* in *Definitions* section of this report) were identified based on onset date, date of previous infection, and previous infection species type: 16 *P. vivax* cases and one *P. ovale* case. Among the 17 relapses, 11 patients (10 *P. vivax* and one *P. ovale*) received primaquine for the most recent infection to avoid future relapses.

Purpose of Travel

Purpose of travel to areas in which malaria is endemic was reported for 597 (91%) of the 659 U.S. civilians with imported malaria. Though travelers could report multiple reasons for travel, the largest proportion (70%) was VFR travelers; the second and third highest proportions, 11% and 7%, were persons who had traveled as missionaries or on business, respectively (Table 6). The proportions of purpose for travel in all categories in 2009 were similar to 2008; however, patients who travelled for tourism decreased significantly, from 10% in 2007 to 5% in 2009. A significant association was identified between purpose of travel and prophylaxis use. Among VFR travelers, 67 (17%, the lowest percentage among cases where purpose of travel was known) used prophylaxis compared with those who traveled for other reasons. No significant association was found between purpose of travel and geographic region

of infection acquisition. No significant association was noted between purpose of travel and species type.

Malaria by Age

Among the 1,364 cases among patients for whom age was known, 225 (16%) occurred in persons aged <18 years, 1,075 (79%) in persons aged 18–64 years, and 64 (5%) in persons ages ≥65 years. Although the majority of cases occur in persons aged 18–64 years, pediatric cases are of particular interest because the preventive care of most children is determined by parents or guardians. Among the 225 cases among persons aged <18 years, 89 (40%) occurred among U.S. civilian children (including one congenital case), 70 (31%) cases among children of persons categorized as having a foreign resident status at the time their malaria infection was acquired (including two congenital cases), and 66 (29%) children of unknown resident status. Of the 89 cases among U.S. civilian children, five (6%) were aged <24 months, 20 (22%) were aged 24–59 months, 39 (44%) were aged 5–12 years, and 25 (28%) were aged 13–17 years. Seventy-nine (89%) of the cases among U.S. civilian children for whom country of exposure was known were attributable to travel to Africa. Among the 81 U.S. civilian children for whom reason for travel was known, 59 (73%) were visiting friends and relatives, 10 (12%) were travelling for educational purposes, six (7%) were travelling for missionary work, and six cases were either tourists or unspecified. Of the 86 children for whom chemoprophylaxis information was known, 27 (31%) were reported as having taken chemoprophylaxis, of whom 18 (67%) had taken an appropriate regimen; however, only four (22%) reported adherence

Treatment in Uncomplicated Imported Malaria Cases

Information on treatment medicines for malaria infection in imported cases was available for 865 (58%) cases. Of these, 734 (85%) were classified as uncomplicated, including 474 (65%) *P. falciparum*, 133 (18%) *P. vivax*, 22 (3%) *P. malariae*, 21 (3%) *P. ovale*, 11 (2%) mixed cases, and 73 (10%) where species type was unknown or unreported. The CDC Guidelines for Treatment of Malaria in the United States (*11*) was used to determine whether the medicines listed for treatment were appropriate.

Of the total 734 patients with uncomplicated cases, the majority (499 [68%]) were treated appropriately according to the CDC Guidelines for Treatment (*11*), 77 (10%) patients indicated other antimalarial drugs in addition to what is recommended by CDC guidelines, and 158 (22%) patients received inappropriate treatment. The patients who indicated receiving antimalarial drugs in addition to the CDC-recommended regimen were considered appropriately treated. However, because the CDC Surveillance report form is not able to capture the sequence of treatment events, it is difficult to understand and characterize the intended purpose of adding additional antimalarial treatment drugs to the regimen. Among the inappropriately treated patients, 11% were treated with a drug that was previously used for chemoprophylaxis before infection (all of whom took appropriate chemoprophylaxis drug regimens for prevention), which could cause potential toxicity and reduced efficacy.

TABLE 6. Number and percentage of imported malaria cases among U.S. civilians, by purpose of travel at the time of acquisition — United States, 2009

Purpose of travel*	No.	(%)
Visiting friends/relatives	417	(63.3)
Missionary or dependent	65	(9.9)
Unknown	62	(9.4)
Business representative	40	(6.1)
Tourism	32	(4.8)
Student/teacher	28	(4.2)
Other	11	(1.7)
Air crew/sailor	4	(0.6)

* Because travelers can identify multiple reasons for the purpose of travel, the total might not equal 100%.

Adequacy of treatment also varied by species. For the 474 *P. falciparum* cases, 408 (86%) patients were treated appropriately according to CDC guidelines, of which 55 (13%) received other antimalarial drugs in addition to CDC recommendations. In addition, 66 (14%) patients were treated with an inappropriate treatment regimen. Among the 22 *P. malariae* cases, 16 (73%) patients were treated appropriately according to CDC guidelines, of which six (38%) received other antimalarial drugs in addition to CDC recommendations. Furthermore, six (27%) patients were treated with an inappropriate treatment regimen.

Among the 133 *P. vivax* cases, 122 (92%) patients were treated with an appropriate antimalarial drug to address their acute infection, of which three (2%) received other antimalarial drugs in addition to the CDC recommendations. Eleven (8%) patients did not receive an appropriate treatment for their acute infection. However, of the 133 patients with *P. vivax* for whom treatment information was reported, only 74 (56%) received primaquine for relapse prevention. Among the 21 *P. ovale* cases, 19 (90%) patients were treated with an appropriate antimalarial drug to address their acute infection, of which one (5%) received other antimalarial drugs in addition to the CDC recommendations. Two (10%) patients did not receive an appropriate treatment for their acute infection. However, of the 21 patients with *P. ovale* cases for whom treatment information was reported, only six (29%) received

primaquine for relapse prevention. Among the 11 mixed cases, all patients were treated appropriately according to CDC guidelines; however, two received other antimalarial drugs in addition to the CDC-recommended regimens. Of the four mixed cases that included at least one relapsing species, two patients received primaquine.

According to the CDC Guidelines for Treatment, a treatment regimen for a *P. falciparum* infection should be used to presumptively treat cases where species is unknown in the interim of identifying the actual infecting species. Among the 73 cases where species was unknown, 63 (86%) patients were treated appropriately according to CDC guidelines, of which 10 (14%) received other antimalarial drugs in addition to CDC recommendations. Ten (14%) patients were treated with an inappropriate treatment regimen.

Severe Malaria

Among the 1,484 reported cases, 142 (10%) were classified as severe malaria, of which four were fatal cases. Approximately 75% of all cases in patients with known resident status were identified in U.S. residents. No significant association was found between age, resident status, prophylaxis use, and severe malaria. The predominant species among the severe cases was *P. falciparum* (86%), which is similar to 2008 (82%). In patients for whom reason for travel was known, 56% of the severe cases were in VFR travelers (not a significant change from 2008), of which 73% specified acquisition from West Africa and 90% were identified as *P. falciparum* infections. Unlike in 2008, a significant association was found between missionary travelers and severe malaria in 2009. Among missionary travelers, 35% (18 of 51) developed severe disease, compared with 16% (82 of 503) of U.S. civilians traveling for other purposes. The majority of severe cases (80%) occurred in persons aged ≥18 years and 13% occurred in children aged <18 years, eight (6%) of whom were aged <3 years. Twenty-eight (20%) persons reported taking a recommended chemoprophylaxis; however, only four reported adherence to the drug regimen, three of whom were using doxycycline and one atovaquone/proguanil for chemoprophylaxis. Although patients could have multiple clinical complications associated with an infection, the largest proportion of patients experienced severe anemia (34%) and renal failure (20%), respectively. Thirty-seven patients were treated with intravenous artesunate provided by CDC through an investigational new drug protocol.

Malaria During Pregnancy

A total of 19 cases of malaria were reported among pregnant women in 2009, representing 4% of cases among all women (n = 478). Although the number of pregnant cases has slightly increased from 2008 to 2009, no significant differences were noted between pregnant women compared with the number of cases in women in terms of species type, reason for travel, or region of infection acquisition. Eight (42%) of the 19 cases occurred among U.S. civilians, seven of whom reported travel to Africa and one to India. Among the six U.S. civilian pregnant women with known reason for travel, five reported visiting friends and relatives and one reported travel related to education. Of the eight cases of malaria reported among U.S. civilian pregnant women, three reported taking malaria chemoprophylaxis; however, none reported adherence to the drug regimen. Six of the eight patients reported were diagnosed with a *P. falciparum* infection, two of which presented with severe malaria. No information was available on the birth outcomes of the pregnant women.

Selected Malaria Case Reports

Congenital Malaria

Three possible congenital cases, caused by transmission of parasites from mother to child during pregnancy or perinatally during labor, were reported in 2009. Clinical and laboratory data are limited.

Case 1 and 2. Twin infants were born to a surrogate mother in India on November 20. The mother reported history of malaria infection with unidentified species; date of diagnosis was unknown. The mother had an emergency C-section at 31-weeks after which the infants were immediately transferred to the intensive care unit (ICU) at the local hospital in India. The adoptive parents picked up the children from the hospital and returned to the United States 2 weeks after birth. Both infants developed symptoms of malaria on December 23 and were found to have severe anemia. One child was identified with a *P. falciparum* infection; however, the species that infected the second child was unknown. Both children were treated with quinidine, clindamycin, and blood transfusions. Because they spent the first 2 weeks of life in India before traveling to the United States, it is possible that these twins acquired malaria infection via mosquito bite in India soon after birth.

Case 3. On July 7, a 5-month old infant was admitted to the hospital ICU for treatment of *P. vivax* malaria. The infant had no travel history; however, the mother had traveled to India 1.5 years earlier but her malaria staus was unknown. The child was treated with mefloquine and primaquine.

Transfusion/Transplant Transmitted Infections

Case 1. A case of stem-cell transplant transmitted malaria was identified at the clinical treatment unit of the National Institutes of Health. The patient was a female who was originally from West Africa but had been in the United States since

2007. In addition to receiving the stem-cell transplant, which was donated by her brother who had lived in West Africa 3 months before donation, on November 19, she had received red blood cell transfusions from seven different donors. On December 4, the patient developed fever and rigors and was found to be positive by blood film and PCR-confirmed for *P. falciparum*. All seven blood donors were screened with a travel questionnaire and had no recent travel to countries where malaria is endemic. In addition, all seven had negative antibody tests for malaria. During her brother's preparation for stem cell donation, he had three blood smears that did not demonstrate parasitemia. However, after donation, the brother was tested again and was found to be positive for *P. falciparum* through serologic testing. A month later, repeat testing on an archived sample of the brother's blood before stem cell donation was found to be positive by PCR. The donor was treated and follow up PCR was negative. The patient was treated with malarone and recovered.

Case 2. On June 21, a 27-year-old man had onset of extreme fatigue, fever, diarrhea, and incontinence. On July 2, malaria caused by *P. falciparum* was diagnosed by positive blood smear. The patient reported no travel history outside of Florida. He had received multiple transfusions during May 16–June 8. The patient was treated with malarone and recovered. Sixteen of the 23 donors were contacted by the blood bank performing the investigation. Among the donors was a 27-year-old man who emigrated from Nigeria in 2004 and who reported having malaria at age 12 years. He had been treated at that time and had no symptoms of malaria since. A specimen sent to CDC was PCR negative, but the donor did have malaria antibodies detectable by IFA. According to the Florida department of health, the donor was counseled by the local blood bank and was instructed to seek medical attention and treatment.

Case 3. On October 12, a 78-year-old man from New Jersey receiving chemotherapy for lung cancer had severe anemia diagnosed (hemoglobin: 4.8). Further evaluation of his anemia revealed *P. falciparum* on blood smears. The patient denied any travel out of the country during the preceding year. However, he had received numerous blood transfusions to treat chemotherapy-related anemia in the 12 months before admission. A total of nine units had been transfused; two units were transfused in December 2008, three units in January 2009, two units in August 2009, and two units in September 2009. The patient was treated with quinine and clindamycin, recovered from his malaria, and was discharged on November 12, 2009. The blood center, in collaboration with the Health Department, conducted a donor traceback investigation. The investigation found that one donor was a 30-year-old woman from New Jersey who had travelled to China, Uganda, and Brazil 13–17 months before the donation. The donor had lived in Uganda and Tanzania as a child but had immigrated to the United States. PCR performed on the blood sample provided by the donor was negative, but malaria antibodies were detectable by IFA.

Deaths Attributed to Malaria

Four deaths attributable to malaria were reported in 2009 and are described in the following case reports.

Case 1. A 71-year-old man with a history of hypertension, diabetes, and coronary artery disease was visiting the United States from India. He arrived on September 11, 2009, and was already experiencing symptoms. On September 14, he was seen at an emergency department and was admitted for treatment of what was thought to be a urinary tract infection. While hospitalized, he also developed hyponatremia and a decreased level of consciousness. On September 16, *P. falciparum* was diagnosed by blood smear (3.4% parasitemia), and he was transferred to the ICU. Quinidine (loading dose) was administered after determining that the QT interval was normal. During intravenous infusion of quinidine, a cardiac arrest occurred. Following a protracted resuscitation, acute tubular necrosis and ARDS were diagnosed. The quinidine infusion was discontinued and intravenous artesunate, provided by CDC, was successfully initiated. Despite a progressive decline to 0% parasitemia, the patient continued to deteriorate and died on September 18, 2009.

Case 2. A 61-year-old woman who had been working as an anthropologist in the eastern Congo for 2 weeks returned to the United States on June 25, 2009. She had not used malaria chemoprophylaxis. Her onset of illness was approximately July 3, and although she sought medical care, no diagnosis or treatment was provided. The patient arrived in the emergency department by ambulance on July 9 with fever, weakness, nausea, vomiting, and diarrhea. On initial assessment, she was lucid and oriented. About 2.5 hours later, she was disoriented and lethargic. Initial workup revealed infection with *P. falciparum* with a 62% parasitemia as well as acute renal failure, jaundice, thrombocytopenia, and severe metabolic acidosis. She was admitted to the ICU and started on a regimen of intravenous quinidine and doxycycline. She also received an exchange transfusion and additional units of blood afterward (total: 17 units). By July 10, her parasitemia had decreased to 10%; however, on her ECG, her QTc interval had increased to >25% of baseline, a sign of quinidine toxicity. Hypotension and acidosis (pH<7.0 by arterial blood gas analysis) persisted, requiring numerous pressors and repeated doses of sodium bicarbonate. She had a respiratory arrest necessitating intubation and mechanical ventilation. CDC was contacted and artesunate treatment was recommended. By July 11, her parasitemia had decreased to 2% but her pupils had become fixed and dilated.

At the request of her family her status was changed to "Do Not Resuscitate." That evening, she developed ventricular arrhythmias and died.

Case 3. A 33-year-old woman who traveled to Burkina Faso annually to study traditional herbal medicines experienced onset of chills, fever, and headache during a flight when returning to the United States on August 15. Her medical history was notable for malaria infection previously, which was self treated with medicines purchased in Africa and herbal teas. On September 1, she sought medical attention and stated that she had self-treated with herbal teas. In the emergency department, she was hypotensive (blood pressure: 85/46mmHg) and tachycardic (heart rate: 120bpm) with severe anemia (hemoglobin: 4.5g/dL). A diagnosis of malaria was made by blood film, and the patient was immediately started on intravenous quinidine and doxycycline along with multiple transfusions of blood products. The patient developed bradycardia, which did not respond to atropine. She died within 8 hours of admission to the hospital.

Case 4. A 43-year-old man visiting the United States from Zimbabwe was admitted to the emergency department on June 2, 2009, complaining of abdominal pain and lethargy. Within 40 minutes of arrival, the patient had a seizure and became unresponsive. He was intubated and sent for head and abdominal CT scans, which revealed no acute disease. Peripheral smear was positive for *P. falciparum* at 8% parasitemia. The patient was started on doxycycline and clindamycin; no quinidine was available in the hospital. Later that evening, intravenous quinidine was acquired and administered. He developed refractory hypotension on the night of June 3 and required multiple vasopressors. The patient's neurologic status never improved, and a repeat CT scan of the head revealed cerebral edema. He died on June 5, 2009.

Discussion

The baseline number of malaria cases during the preceding 4 years has remained unchanged. The number of cases reported in 2009 is similar to the average number of cases (1,473) reported during the preceding 4 years; however, the number of cases reported in 2009 increased 14% over the 1,298 cases reported in 2008. Additional reductions in malaria cases will require emphasizing the importance of prescribing and adhering to appropriate preventive measures for malaria, seeking prompt medical attention when fever develops after traveling to a malarious area, and educating clinicians on appropriate diagnostic and treatment guidelines for malaria.

A key strategy in decreasing imported malaria cases is prevention of malaria in travelers. In 2009, a majority of the patients did not take prophylaxis before travel (including 80% of pediatric cases), and only a third adhered to what was prescribed. Travelers need to be more aware of required preventive measures when traveling in areas where malaria is endemic, and clinicians need to prescribe appropriate medications and emphasize that the drug adherence is critical. Surveillance data suggest that malaria prevention messages should be targeted towards VFRs and missionaries, groups among whom prophylaxis use was lowest. Health prevention messages targeted toward VFR populations have been an important focus because of the substantially increased risk for travel-related illness (*12,13*). Among missionary workers, only one person was identified as being adherent to a recommended chemoprophylaxis regimen, and missionary work was significantly associated with having severe malaria. Because many missionary volunteers work in areas where malaria is endemic and sometimes develop behavior patterns that could increase the risk for illness (*14,15*), focused prevention messages could help improve prophylaxis use and prevent serious illness.

Another population requiring targeting of malaria prevention messages is pregnant travelers because of the high risk for maternal and perinatal morbidity and mortality (*16*). In 2009, a total 19 cases of malaria were reported among pregnant women and three congenital malaria cases. Of the 19 cases in pregnant women, two had severe malaria, and none reported adherence to the chemoprophylaxis drug regimen. Pregnant travelers should be counseled to avoid travel to malarious areas. If deferral of travel is impossible, pregnant women should be informed that the risks for malaria greatly outweigh those associated with prophylaxis and that safe chemoprophylaxis regimens are available and should be emphasized. Specific guidance for pregnant travelers is available online (http://wwwnc.cdc.gov/travel/yellowbook/2010/chapter-8/traveling-while-pregnant.aspx).

Despite reported adherence to appropriate prophylaxis, 34 (33% of those for whom adherence was reported) persons developed malaria. However, it is difficult to determine whether illness developed because of malabsorption of the antimalarial drug or emerging drug resistance or if reporting of adherence was accurate. No evidence exists to indicate increasing rates of failure among any of the recommended chemoprophylactic regimens. However, to confirm and assess reasons for chemoprophylaxis failure, health-care providers are encouraged to contact CDC immediately if they suspect chemoprophylaxis failure. CDC can assist with measuring blood drug levels to assess adherence to prophylactic medications and in vitro parasite response to antimalarials to determine if resistance is present.

Reducing the risk for severe morbidity and mortality from malaria depends on ill travelers seeking immediate medical attention when they develop fever, whether or not prophylaxis

was taken. Clinicians should include malaria in the differential diagnosis of fever for any traveler returning from a malarious area. Signs and symptoms of malaria are often nonspecific, but fever usually is present. Other symptoms can include headache, chills, increased sweating, back pain, myalgia, diarrhea, nausea, vomiting, and cough. Clinicians should ask all febrile patients for a travel history, including international visitors, immigrants, refugees, and migrant laborers. Any delay in the correct diagnosis and treatment of malaria can result in complications, even if an appropriate treatment regimen is used.

Treatment should be determined on the basis of several key factors, including the probable geographic origin of the parasite, the *Plasmodium* species, parasite density, and the patient's clinical status (*17*). Geographical distribution of species can change over time. For example, previous studies have shown that the prevalence of *P. vivax* in West Africa is very rare because of the general lack of the Duffy antigen among West Africans (*18*). However, in 2009, malaria caused by *P. vivax* was reported in four U.S. travelers to West Africa. Explanations for these infections might include incorrect species identification by the reporting laboratories or a higher prevalence of *P. vivax* in West Africa than had been previously recognized (*19–22*). All instances of possible *P. vivax* infections acquired in West Africa should be confirmed by PCR to confirm the *Plasmodium* species and help monitor the epidemiology of *P. vivax* infection. Furthermore, PCR should be used in all instances where speciation cannot be determined by microscopy. Certain reference laboratories and health departments have the capacity to perform PCR for species identification; however, if PCR is not available or additional diagnostics are needed, CDC can provide assistance.

The majority of uncomplicated malaria cases reported in 2009 were treated according to the CDC treatment guidelines. However, among cases where an inappropriate treatment regimen was reported, 11% were treated with a drug that had already been used for chemoprophylaxis. Using an inappropriate treatment regimen can extend the duration and severity of the patient's illness and potentially cause toxicity. Health-care providers should obtain information on prior chemoprophylaxis use to determine the most effective and appropriate treatment. If a diagnosis of malaria is strongly suspected and cannot be confirmed, or if a diagnosis of malaria is confirmed but species determination is not possible, antimalarial treatment should be initiated that is effective against *P. falciparum*. Resistance of *P. falciparum* to chloroquine is worldwide, with the exception of a limited number of geographic regions (e.g., Haiti and Central America). Therefore, therapy for presumed *P. falciparum* malaria should include drugs effective against such resistant strains (*17*). Prompt treatment of suspected malaria is essential, particularly for persons with *P. falciparum* infection, who are at much higher risk for experiencing life-threatening complications soon after the onset of illness.

For all *P. vivax* and *P. ovale* cases, *CDC Guidelines for Treatment* advise that primaquine should be included as a part of the treatment protocol. However, of the 74 uncomplicated *P. vivax* and *P. ovale* infections in which CDC treatment guidelines were not followed, 82% did not have primaquine included in their reported treatment regimen. Also, of the 17 cases that were categorized as a probable relapse case, only 11 were treated with primaquine for their most recent infection. *P. vivax* and *P. ovale* form hypnozoites (parasite stages in the liver that can result in multiple relapses of infection) that can cause persistent infection and relapse of illness weeks to months after the primary infection. Therefore, treatment of *P. vivax* and *P. ovale* infections should be aimed at addressing both the blood and liver stage of infection, thereby preventing relapses. However, the use of primaquine in *P. vivax* and *P. ovale* cases could be underestimated because of underreporting of treatment regimens (e.g., the reporting form was sent in before primaquine was known to be prescribed, or while awaiting G6PD[†] results that are needed before primaquine can be used). Health-care providers should consult the *CDC Guidelines for Treatment*, which are updated frequently, and contact the CDC's Malaria Hotline (770-488-7788) for case management advisement when needed.

The last reported transfusion/transplant related malaria case was in 2007; in 2009 there were three cases. Malaria cases transmitted by blood transfusion or organ transplantation are rare in the United States; however no approved tests are available in the United States to screen donated blood, stem cells, or organs for malaria. In investigating transfusion/transplantation transmitted cases, infected donors are most often identified by antibody tests since low parasitemia can be sometimes below the level of detection through PCR or smear microscopy (*23*). Prevention of transfusion and transplant related malaria requires careful questioning of prospective donors. Screening guidelines from the Food and Drug Administration (FDA) recommend that travelers to an malaria endemic area should be deferred from donating blood for 1 year after their return. Former residents of areas where malaria is present should be deferred for 3 years and persons diagnosed with malaria should be deferred 3 years after treatment, during which time they must have remained free of symptoms of malaria (*24*).

Patients with suspected or confirmed malaria who are severely ill should be treated aggressively with parenteral

[†] Primaquine is not recommended for those who are glucose-6-phosphate-dehydrogenase (G6PD) deficient, because primaquine can cause hemolysis and even death in G6PD deficient persons. Normal G6PD levels must be documented before using primaquine for either chemoprophylaxis or treatment.

antimalarial therapy regardless of the species of malaria identified on the blood smear. Quinidine gluconate continues to be recommended for parenteral malaria therapy. However, this drug is no longer available in some hospitals because newer antiarrhythmic drugs with lesser side effects are being used. In addition, parenteral quinidine gluconate is potentially cardiotoxic and should be administered in an intensive care setting with continuous cardiac and frequent blood pressure monitoring. Intravenous artesunate is an alternative to quindine gluconate, is highly effective for treating severe malaria, and is available as an investigational new drug (IND) through CDC. Artesunate is stocked at nine sites around the United States and can be rapidly shipped for free to clinicians on request. Certain guidelines and eligibility requirements must be met to enroll a patient in the treatment protocol. Physicians who administer the drug must notify CDC of any adverse event after administration and comply with the IND protocol (*25*). To enroll a patient with severe malaria in this treatment protocol, health-care providers can call the CDC Malaria Hotline during regular business hours (Table 7). During evenings, weekends, and holidays, callers should telephone the CDC Emergency Operations Center (Table 7) and ask to speak with a CDC Malaria Branch clinician.

Travelers and health-care providers are encouraged to use CDC's resources on malaria prevention and treatment and contact the CDC Malaria Branch for assistance with diagnostic or case management needs. Detailed recommendations for preventing malaria are available to the general public online (http://wwwnc.cdc.gov/travel/yellowbook/2010/chapter-2/malaria.aspx#990). Additional information on malaria prevention recommendations is also available through the online CDC malaria map application (http://www.cdc.gov/malaria/map). The interactive map allows the user to search or browse countries, cities, and place names and get information about malaria in a particular location and see recommended malaria prophylaxis for certain areas. In addition, CDC biannually publishes recommendations in *Health Information for International Travel* (i.e., *The Yellow Book*), which is available and updated on the CDC Travelers' Health site and is also available for purchase (Table 7).

Health-care providers should be familiar with prevention, recognition, and treatment of malaria and are encouraged to consult appropriate sources for malaria prevention and treatment recommendations (Table 7). Physicians seeking assistance with the diagnosis (including telediagnosis) or treatment of patients with suspected or confirmed malaria should call CDC's Malaria Hotline during regular business hours or CDC's Emergency Operations Center during evenings, weekends, and holidays. Information also is available from CDC online (http://www.cdc.gov/malaria/diagnosis_treatment/index.html). These resources are intended for use by health-care providers only.

TABLE 7. Sources for malaria prophylaxis, diagnosis, and treatment recommendations

Type of information	Source	Availability	Telephone number, Internet address, or electronic mail address
Prophylaxis	CDC's Traveler's Health internet site (includes online access to *Health Information for International Travel*)	24 hours/day	http://wwwnc.cdc.gov/travel/
Prophylaxis	*Health Information for International Travel*, (*The Yellow Book)*	Order from Oxford University Press, Inc. Order Fulfillment 198 Madison Avenue New York, NY 10016-4314	800-451-7556 or www.oup.com/us/
Prophylaxis	CDC Malaria Map Application	24 hours/day	http://www.cdc.gov/malaria/map/
Diagnosis	CDC's Division of Parasitic Diseases and Malaria diagnostic internet site (DPDx)	24 hours/day	http://www.dpd.cdc.gov/dpdx
Diagnosis	CDC's Division of Parasitic Diseases and Malaria diagnostic CD-ROM (DPDx)	Order by electronic mail from CDC Division of Parasitic Diseases and Malaria	dpdx@cdc.gov
Treatment*	CDC's Malaria Branch	9:00 am- 5:00 pm Eastern Time, Monday- Friday	770-488-7788*
Treatment*	CDC's Malaria Branch	5:00 pm- 9:00 am Eastern Time on weekdays and all day weekends and holidays	770-488-7100* (This is the number for the CDC's Emergency Operations Center. Ask staff member to page person on call for Malaria Branch) http://www.cdc.gov/malaria/diagnosis_treatment/treatment.html

* These telephone numbers are intended for use by health-care professionals only.

Acknowledgments

The authors acknowledge the state, territorial, and local health departments; health-care providers; and laboratories for reporting this information to CDC.

References

1. World Health Organization. World malaria report 2009. WHO Press. 2009.
2. Cox-Singh J, et al. *Plasmodium knowlesi* malaria in humans is widely distributed and potentially life threatening. Clin Infect Dis. 2008 Jan 15; 46(2):172-3.
3. Pan American Health Organization. Report for registration of malaria eradication from United States of America. Washington, DC: Pan American Health Organization; 1969.
4. CDC. Multifocal autochthonous transmission of malaria—Florida, 2003. MMWR 2004;53:412–3.
5. CDC. National Notifiable Diseases Surveillance System. November 10, 2009. http://www.cdc.gov/ncphi/disss/nndss/nndsshis.htm
6. World Health Organization. Terminology of malaria and of malaria eradication: report of a drafting committee. Geneva, Switzerland: World Health Organization; 1963:32.
7. World Health Organization. Diagnosis and management of Severe Malaria. Geneva, Switzerland: World Health Organization; 2006. Available at http://whqlibdoc.who.int/hq/2000/WHO_CDS_CPE_SMT_2000.4_Part1.pdf.
8. CDC. Malaria surveillance—United States, 2008. MMWR 2010;59 (No. SS-7).
9. CDC. Malaria Rapid Diagnostic Test. MMWR 2007;56:686.
10. BinaxNOW® Malaria [package insert]. Scarborough, Maine: Inverness Medical Professional Diagnostics; 2007.
11. CDC. Guidelines for treatment of malaria in the United States. Available at http://www.cdc.gov/malaria/resources/pdf/treatmenttable73109.pdf.
12. Bacaner N, Stauffer B, Boulware D, Walker P, Keystone JS. Travel medicine considerations for North American immigrants visiting friends and relatives. JAMA 2004;291:2856–64.
13. Angell SY, Cetron MS. Health disparities among travelers visiting friends and relatives abroad. Ann Intern Med 2005;142:67–72.
14. Arguin PM, et al. Survey of rabies preexposure and postexposure prophylaxis among missionary personnel stationed outside the United States. J Travel Med. 2000 Jan;7(1):10-4.
15. Burdon J. Use of malarial prophylaxis amongst a population of expatriate church workers in Northeast Zaire. J Travel Med. 1998 Mar;5(1):36-8.
16. Griffith KS, Lewis LS, Mali S, Parise ME. Treatment of malaria in the United States: A systematic review. JAMA 2007;297:2264–76.
17. Baird JK. Effectiveness of antimalarial drugs. N Engl J Med 2005;352: 1565–77.
18. Miller LH, et al. The resistance factor to *Plasmodium vivax* in blacks: the Duffy-blood-group genotype, FyFy. N Engl J Med 1979;295:302–4.
19. Ryan J R, Stoute JA, Amon J, et al. Evidence for transmission of *Plasmodium vivax* among Duffy antigen negative population in Western Kenya. Am J Med Hyg 2006;75:575–81
20. Culleton R, Ndounga M, Zeyrek FY, et al. Evidence for the transmission of *Plasmodium vivax* in the Republic of the Congo, West Central Africa. J Infect Dis 2009;200:1465–9
21. Menard D, Barnadas C, Bouchier C, et al. *Plasmodium vivax* clinical malaria is commonly observed in Duffy-negative Malagasy people. Proc Natl Acad Sci U S A 2010;107: 5967–71
22. Cavasini CE, Mattos LC, Bonini-Domingos CR, et al. *Plasmodium vivax* infection among Duffy antigen-negative individuals from the Brazil Amazon region: an exception? Trans R Soc Trop Med Hyg 2007;101: 1042–4.
23. Mungai, M, Tegtmeier G, Chamberland M, Parise M. Transfusion-transmitted malaria in the United States from 1963 through 1999. N Engl J Med 2001;344:1973–8
24. CDC. Blood donor screening. Available at http://www.cdc.gov/malaria/blood_banks.html.
25. CDC. New medication for severe malaria available under an investigational new drug protocol. MMWR 2007;56;769–70.

The *Morbidity and Mortality Weekly Report (MMWR)* Series is prepared by the Centers for Disease Control and Prevention (CDC) and is available free of charge in electronic format. To receive an electronic copy each week, visit MMWR's free subscription page at *http://www.cdc.gov/mmwr/mmwrsubscribe.html*. Paper copy subscriptions are available through the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402; telephone 202-512-1800.

Address all inquiries about the *MMWR* Series, including material to be considered for publication, to Editor, *MMWR* Series, Mailstop E-90, CDC, 1600 Clifton Rd., N.E., Atlanta, GA 30333 or to *mmwrq@cdc.gov.*

☆ U.S. Government Printing Office: 2011-723-011/21041 Region IV ISSN: 1546-0738