

医薬品 研究報告 調査報告書

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| 販売名(企業名)  | イントロンA(シエリング・プラウ(株))   |                                |  | 米国       |                         |
| 研究報告の概要   | <p>マラリアサーベイランスアメリカ、2002年:<br/>                     CDCは、アメリカ国内で感染した先天的感染の1例、輸血に関連した感染の可能性のある1例の報告を受けた。<br/>                     先天的感染の1症例は、生後3週間の女兒で、2002年8月22日、2日間の摂食不十分と傾眠の症状を訴え入院した。血液フィルムから、三日熱マラリア原虫が赤血球内に寄生していることがわかった。7日間のquinineの投与で完全に回復した。女兒は正常な自然経膾分娩で生まれ、女兒の母親は、以前、ガイアナで働いておりマラリア歴があった。母親の最初のマラリア感染は、1999年4月で、その後、2001年の4月、6月、8月と3回の症状の発現があった。症状が発現している間は、chloroquineかsulfadoxine-pyrimethamineのどちらかが、症状消失まで投与されていた。出産の3日前、母親に発熱、悪寒、ひどい頭痛が見られた。出産した日に提出した血液フィルムにより三日熱マラリア寄生体が見つかった。母親はchloroquineとprimaquineによる治療後、完全に回復した。<br/>                     輸血に関連した感染の可能性のある1例は、貧血と血管形成異常のために赤血球の輸血を定期的に受けている84歳の女性で、2002年6月30日、四日熱マラリアと診断された。ここ4ヵ月間に、この患者に赤血球を輸血したドナーの一人が血清学により四日熱マラリアの可能性が指摘された。この感染ドナーは17歳の男性で、1994年に西アフリカから移住してきており、2002年に献血をした。患者は2002年5月1日に、この血液を輸血された。CDCに送られたこのドナーの血液サンプルから、四日熱マラリア原虫に対する高い免疫蛍光抗体価が検出されたが、寄生体はドナーの血液フィルムからもPCRテストからも検出されなかった。ドナーはかつてのマラリア感染を否定し、以前のマラリア感染を示す歴史もないと報告した。</p> |                                |  |          | 使用上の注意記載状況・<br>その他参考事項等 |
|   | 報告企業の意見  | 今後の対応                          | なし   |          |                         |
| <p>本報告は、母児垂直感染と輸血による感染が疑われる報告であるが、本製品への汚染を示す報告ではなかった。</p> |  | <p>今後とも継続的な情報収集および評価検討を行う。</p> |  |          |                         |

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Surveillance Summaries

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## Malaria Surveillance --- United States, 2002

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### Abstract

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

**Period Covered:** This report covers cases with onset of illness in 2002.

**Description of System:** Malaria cases confirmed by blood film are 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). Data from NMSS serve as the basis for this report.

**Results:** CDC received reports of 1,337 cases of malaria with an onset of symptoms in 2002 among persons in the United States or one of its territories. This number represents a decrease of 3.3% from the 1,383 cases reported for 2001. *P. falciparum*, *P. vivax*, *P. malariae*, and *P. ovale* were identified in 52.3%, 25.4%, 2.8%, and 2.8% of cases, respectively. Eleven patients (0.8% of total) were infected by  $\geq 2$  species. The infecting species was unreported or undetermined in 213 (15.9%) cases. Compared with 2001, the number of reported malaria cases acquired in Asia ( $n = 171$ ) and Africa ( $n = 903$ ) increased by 4.3% and 1.9%, respectively, whereas the number of cases acquired in the Americas ( $n = 141$ ) decreased by 41.2%. Of 849 U.S. civilians who acquired malaria abroad, 317 (37.3%) reported that they had followed a chemoprophylactic drug regimen recommended by CDC for the area to which they had traveled. Five patients became infected in the United States, one through congenital transmission, one probable transfusion-related, and three whose infection cannot be linked epidemiologically to secondary cases. Eight deaths were attributed to malaria. All deaths were caused by *P. falciparum*.

**Interpretation:** The 3.3% decrease in malaria cases in 2002, compared with 2001, resulted primarily from a marked decrease in cases acquired in the Americas, but this decrease was offset somewhat by an increase in the number of cases acquired in Africa and Asia. This limited decrease probably represents year-to-year variation in malaria cases, but also could have resulted from local changes in disease transmission, decreased travel to malaria-endemic regions, fluctuation in reporting to state and local health departments, or an increased use of effective antimalarial chemoprophylaxis. In the majority of reported cases, U.S. civilians who acquired infection abroad were not on an appropriate chemoprophylaxis regimen for the country in which they acquired malaria.

**Public Health Actions:** Additional information was obtained concerning the eight fatal cases and the five infections acquired in the United States. Persons traveling to a malarious area should take one of the recommended chemoprophylaxis regimens appropriate for the region of travel, and travelers should use personal protection measures to prevent mosquito bites. Any person who has been to a malarious area and who subsequently experiences a fever or influenza-like symptoms should seek medical care immediately and report their travel history to the clinician; investigation should include a blood-film test for malaria. Malaria infections can be fatal if not diagnosed and treated promptly. Recommendations concerning malaria prevention can be obtained from CDC by calling the Malaria Hotline at 770-488-7788 or by accessing CDC's Internet site at <http://www.cdc.gov/travel>.

## Introduction

Malaria in humans is caused by infection with one or more of four species of *Plasmodium* (i.e., *P. falciparum*, *P. vivax*, *P. ovale*, and *P. malariae*). The infection is transmitted by the bite of an infective female *Anopheles* species mosquito. Malaria infection remains a devastating global problem, with an estimated 300–500 million cases occurring annually (1). Forty-one percent of the world's population lives in areas where malaria is transmitted (e.g., parts of Africa, Asia, the Middle East, Central and South America, Hispaniola, and Oceania) (1), and 700,000–2.7 million persons die of malaria each year, 75% of them African children (2). 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, water 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 antimalarial drug resistance. Anopheline mosquitos remain seasonally present in all states except Hawaii.

The majority of cases of malaria each year diagnosed in the United States have been imported from regions of the world where malaria transmission is known to occur, although congenital infections and infections resulting from exposure to blood or blood products are also reported in the United States. In addition, a limited number of cases are reported that might have been acquired through local mosquitoborne 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. For example, an increase in *P. falciparum* malaria among U.S. travelers to Africa, an area with increasing chloroquine resistance, prompted CDC to change the recommended chemoprophylaxis regimen from chloroquine to mefloquine in 1990 (5).

The signs and symptoms of malaria illness are varied, but the majority of patients experience fever. Other common symptoms include headache, back pain, chills, increased sweating, myalgia, nausea, vomiting, diarrhea, and cough. The diagnosis of malaria should be considered for persons who experience these symptoms and who have traveled to an area with known malaria transmission. Malaria should also be considered in the differential diagnoses of persons who experience fevers of unknown origin, regardless of their travel history. Untreated *P. falciparum* infections can rapidly progress to coma, renal failure, pulmonary edema, and death. Asymptomatic parasitemia can occur, most commonly among persons who have been long-term residents of malarious areas. This report summarizes malaria cases reported to CDC with onset of symptoms in 2002.

## Methods

### Data Sources

Malaria case data are reported to the National Malaria Surveillance System (NMSS) and the National Notifiable Diseases Surveillance System (NNDSS) (6). Both systems rely on passive reporting, and the numbers of reported cases might differ because of differences in collection and transmission of data. A substantial difference in 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). This report presents only data regarding cases reported to NMSS.

Cases of blood-film-confirmed malaria among civilians and military personnel are identified by health-care providers or laboratories. Each slide-confirmed malaria case is reported to local or state health departments and to CDC on a uniform case report form that contains clinical, laboratory, and epidemiologic information. CDC staff review all report forms 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. Cases reported directly to CDC are shared with the relevant state health department. All cases that have been acquired in the United States are investigated, including all induced and congenital cases and possible introduced or cryptic cases. Information derived from uniform case report forms is entered into a database and analyzed annually.

### Definitions

The following definitions are used in this report:

- Laboratory criteria for diagnosis: Demonstration of malaria parasites in blood films.

- **Confirmed case:** Symptomatic or asymptomatic infection that occurs in a person in the United States who has microscopically confirmed 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 if the indicated *Plasmodium* species differs from the initially identified species. A subsequent episode of malaria occurring in a person while in the United States could indicate a relapsing infection or treatment failure resulting from drug resistance if the indicated *Plasmodium* species is the same species identified previously.

This report also uses terminology derived from the recommendations of the World Health Organization (7). 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 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 (Puerto Rico, Guam, and the U.S. Virgin Islands).
- **Induced malaria:** Malaria acquired through artificial means (e.g., blood transfusion or by using shared common syringes).
- **Relapsing malaria:** Renewed manifestations (i.e., clinical symptoms or parasitemia) of malarial infection that is separated from previous manifestations of the same infection by an interval greater than the usual periodicity of the paroxysms.
- **Cryptic malaria:** An isolated malaria case that cannot be linked epidemiologically to secondary cases.

### Microscopic Diagnosis of Malaria

The early and prompt diagnosis of malaria requires that physicians 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. Thick and thin blood films must be prepared correctly because diagnostic accuracy depends on blood-film quality and examination by experienced laboratory personnel\* ([Appendix](#)).

## Results

### General Surveillance

For 2002, CDC received 1,337 malaria case reports occurring among persons in the United States and its territories, representing a 3.3% decrease from the 1,383 cases reported with a date of onset in 2001 (8). This incidence is the sixth highest number of reported cases since 1980 and represents the second highest number of U.S. civilian cases reported in the previous 30 years ([Table 1](#)). In 2002, a total of 849 cases occurred among U.S. civilians, compared with 891 cases reported for 2001; the number of cases among foreign civilians decreased from 316 cases to 272 ([Table 1](#)). During 1997--2001, an increase in cases among U.S. civilians has occurred, but cases among foreign civilians have decreased ([Figure 1](#)). Cases among U.S. military personnel increased from 18 to 33 in 2002. For 183 cases, information was insufficient to determine civilian or military status.

### *Plasmodium* Species

The infecting species of *Plasmodium* was identified in 1,124 (84.1%) of the cases reported in 2002. *P. falciparum* and *P. vivax* were identified in blood films from 52.3% and 25.4% of infected persons, respectively ([Table 2](#)). The 699 *P. falciparum* cases reported for 2002 represented a 0.8% increase from the 693 cases in 2001, and the number of *P. vivax* infections decreased by 11.9% (from 385 in 2001 to 339 in 2002). Among 1,044 cases in which both the region of acquisition and the infecting species were known, 81.7% of infections acquired in Africa were attributed to *P. falciparum*; 9.5% were attributed to *P. vivax*. The converse was true of infections acquired in the Americas and Asia: 70.0% and 82.8% were attributed to *P. vivax*, and only 26.2% and 11.5% were attributed to *P. falciparum*, respectively.

### Region of Acquisition and Diagnosis

All but five reported cases (n = 1,332) were imported. Of 1,252 imported cases in which the region of acquisition was known, the majority (72.1%; n = 903) were acquired in Africa; 13.7% (n = 171) and 11.3% (n = 141) were acquired in Asia and the Americas, respectively ([Table 3](#)). A limited number of imported cases were acquired in Oceania (3.0%; n = 37). The highest concentration of cases acquired in Africa came from countries in West Africa (69.7%; n = 629); a substantial percentage of cases acquired in Asia came from the Indian subcontinent (52.6%; n = 90). From within the Americas, the majority of cases were acquired in Central America and the Caribbean (68.1%; n = 96), followed by South America (24.8%; n = 35) and Mexico (7.1%; n = 10). Information regarding region of acquisition was missing for 80 (6.4%) of the imported cases. Compared with 2001, the number of reported malaria cases acquired in Asia and Africa increased by 4.3% and 1.9%, respectively, and the number of cases acquired in the Americas decreased by 41.2%.

In the United States, the five health departments reporting the highest number of malaria cases were New York City ( $n = 202$ ), California ( $n = 197$ ), Maryland ( $n = 101$ ), Florida ( $n = 87$ ), and Texas ( $n = 67$ ) (Figure 2). Whereas the majority of these health departments reported an increase in cases compared with 2001, an overall decrease in cases occurred nationwide. This decrease probably represents year-to-year variation in malaria cases rather than a trend but could also have resulted from local changes in disease transmission, decreased travel to malaria-endemic regions, fluctuation in reporting to state and local health departments, or an increased use of effective antimalarial chemoprophylaxis.

### Interval Between Arrival and Illness

The interval between date of arrival in the United States and onset of illness and the infecting *Plasmodium* species were known for 681 (51.1%) of the imported cases of malaria (Table 4). Symptoms began before arrival in the United States for 92 (13.5%) persons, whereas symptoms began after arrival in the United States for 589 (86.5%) of these patients. Clinical malaria developed within 1 month after arrival in 385 (79.9%) of the 482 *P. falciparum* cases and in 57 (36.8%) of the 155 *P. vivax* cases (Table 4). Only seven (1.0%) of the 681 persons became ill >1 year after returning to the United States.

### Imported Malaria Cases

#### Imported Malaria Among U.S. Military Personnel

In 2002, a total of 33 cases of imported malaria were reported among U.S. military personnel. These cases were reported by state health departments. Of the 28 cases for whom information regarding chemoprophylaxis use was available, 19 (67.9%) patients were not using any chemoprophylaxis.

#### Imported Malaria Among Civilians

A total of 1,121 imported malaria cases were reported among civilians. Of these, 849 (75.7%) cases occurred among U.S. residents, and 272 (24.3%) cases occurred among residents of other countries (Table 5). Of the 849 imported malaria cases among U.S. civilians, 641 (75.5%) had been acquired in Africa, an increase of 1.1% from cases reported in 2001. Asia accounted for 89 (10.5%) cases of imported malaria among U.S. civilians, and travel to the Central American and Caribbean regions accounted for an additional 57 (6.7%) cases. Of the 272 imported cases among foreign civilians, the majority of cases were acquired in Africa (66.2%;  $n = 180$ ).

### Antimalarial Chemoprophylaxis Use

#### Chemoprophylaxis Use Among U.S. Civilians

Information concerning chemoprophylaxis use and travel area was known for 799 (94.1%) of the 849 U.S. civilians who had imported malaria. Of these 799 persons, 482 (60.3%) had not taken any chemoprophylaxis, and 136 (17.0%) had not taken a CDC-recommended drug for the area visited (9). Only 167 (20.9%) U.S. civilians had taken a CDC-recommended medication (9). Data for the specific drug taken were missing for the remaining 14 (1.8%) travelers. A total of 110 (65.9%) patients on CDC-recommended prophylaxis had reported taking mefloquine weekly; 30 (18.0%) had taken doxycycline daily; nine (5.4%) had taken atovaquone-proguanil daily; and six (3.6%) who had traveled only in areas where chloroquine-resistant malaria has not been documented had taken chloroquine weekly. Information on adherence to the drug regimen for these persons is presented in the following section. Twelve patients (7.2%) had taken combinations of drugs that included >1 CDC-recommended drug for the travel region. Of the 136 patients taking a nonrecommended drug, 67 (49.3%) reported taking chloroquine either alone or in combination with another ineffective drug during travel to an area where chloroquine resistance has been documented.

#### Malaria Infection After Recommended Prophylaxis Use

A total of 185 patients (i.e., 167 U.S. civilians, eight persons in the U.S. military, three foreign civilians, and seven persons whose information regarding their status was missing) experienced malaria after taking a recommended antimalarial drug for chemoprophylaxis. Information regarding infecting species was available for 158 (85.4%) patients taking a recommended antimalarial drug; the infecting species was undetermined for the remaining 27.

**Cases of *P. vivax* or *P. ovale* After Recommended Prophylaxis Use.** Of the 185 patients who experienced malaria after recommended chemoprophylaxis use, 69 cases (37.3%) were caused by *P. vivax* and 13 (7.0%) by *P. ovale*. Twenty-two (26.8%) of these 82 patients were noncompliant with antimalarial chemoprophylaxis.

A total of 41 (50.0%) cases of *P. vivax* or *P. ovale* occurred >45 days after arrival in the United States. These cases were consistent with relapsing infections and, thus, do not indicate primary prophylaxis failures. Information was insufficient, because of missing data regarding symptom onset or return date, to assess whether 28 cases were relapsing infections. Thirteen cases, 10 by *P. vivax* and three by *P. ovale*, occurred <45 days after the patient returned ( $n = 9$ ) or before return ( $n = 4$ ) to the United States. Six of the 13 patients were known to be noncompliant with their antimalarial chemoprophylaxis regimen, and four patients were not known to be noncompliant. The region of acquisition varied for the four patients who were not known to be noncompliant (one from East Africa,

one from West Africa, one from Central Africa, and one from Asia). The remaining three patients reported compliance with an antimalarial chemoprophylaxis regimen. Of these three, two had traveled to Papua New Guinea and one to sub-Saharan Africa. Two of these patients reported taking mefloquine, and one reported using doxycycline. Blood samples for serum drug levels were not available for these three patients. The possible explanations for these cases include inappropriate dosing, noncompliance that was not reported, malabsorption of the drug or emerging parasite resistance.

**Cases of *P. falciparum* and *P. malariae* after Recommended Prophylaxis Use.** The remaining 103 cases of malaria reported among persons who had taken a recommended antimalarial drug for chemoprophylaxis include 69 cases of *P. falciparum*, six cases of *P. malariae*, one case of mixed infection, and 27 cases in which the infecting species was unidentified.

A total of 61 of the 69 *P. falciparum* cases among those who reported taking a recommended antimalarial drug were acquired in Africa, five in Asia, and three in Oceania. In 42 (60.9%) of these 69 cases, noncompliance with antimalarials was reported. In five (7.2%) of these 69 cases, patients reported compliance with antimalarial chemoprophylaxis. All five of these patients had traveled to Africa. Of the four who had traveled to West Africa, three had traveled to Ghana and one to Sierra Leone. Three had reported taking mefloquine, and two had reported taking atovaquone-proguanil for malaria chemoprophylaxis. A mefloquine blood level was available for one of the patients who had traveled to Ghana; this patient's mefloquine level was undetectable, thus indicating either noncompliance with the recommended regimen or complete malabsorption of the drug. Blood samples were not available for the remaining four patients who reported compliance with a recommended regimen. Twenty-two cases occurred of *P. falciparum* for which patient compliance was unknown. The majority of these cases were acquired in Africa (n = 19): 11 in West Africa, three in East Africa, two in Central Africa, and three in an unspecified African region. Three cases were acquired outside Africa: one in Indonesia and two in Papua New Guinea. Blood samples were not available for the 22 patients whose compliance status was unknown.

Five of the six *P. malariae* cases among those who reported taking a recommended antimalarial drug were acquired in Africa. In three (50.0%) of these six cases, noncompliance with antimalarials was reported. One (16.7%) case reported compliance with a recommended chemoprophylaxis regimen using doxycycline. This patient traveled to southern Africa and became ill before returning to the United States. In the two remaining cases, patient compliance with prophylaxis was unknown and blood samples were not available; both had traveled in Africa.

#### Purpose of Travel

Purpose of travel to malaria-endemic areas was reported for 745 (87.8%) of the 849 U.S. civilians with imported malaria (Table 6). Of the U.S. civilians with malaria, the largest proportion (45.0%) were persons who had visited friends or relatives in malarious areas; the second and third highest proportion, 10.6% and 10.2%, had traveled to do missionary work and for tourism, respectively.

#### Malaria During Pregnancy

A total of 32 cases of malaria were reported among pregnant women in 2002, representing 7.4% of cases among women. Twelve of the 32 (37.5%) were among U.S. civilians. Six of these twelve women had traveled to visit friends and relatives; seven had traveled in Africa, and five in Asia. A total of 28.1% of pregnant women and 28.7% of nonpregnant women reported taking malaria chemoprophylaxis.

#### Malaria Acquired in the United States

##### Congenital Malaria

One case of congenital malaria was reported in 2002 and is described in the following case report:

- **Case 1.** On August 22, 2002, a full-term female, age 3 weeks, was admitted to a local hospital with a 2-day history of inadequate feeding and somnolence. She had had suspected meconium aspiration and sepsis at birth. At that time, she was admitted to the neonatal intensive care unit. All cultures were negative, and she was discharged from the hospital at age 3 days. At the time of the subsequent admission, her physical examination was normal. Laboratory examination revealed thrombocytopenia (85,000/mm<sup>3</sup>). Blood, urine, and cerebrospinal fluid cultures were obtained, and the patient was treated with ampicillin and cefotaxime. A blood film indicated intraerythrocytic parasites consistent with *P. vivax*. She recovered completely after treatment with quinine for 7 days. The infant had been born via normal spontaneous vaginal delivery to a mother who had worked in Guyana and who had a history of malaria. The mother's first episode of malaria was in April 1999, with three subsequent episodes in April, June, and August 2001. During the episodes, she was treated with either chloroquine or sulfadoxine-pyrimethamine, with complete resolution of symptoms. Three days before giving birth, the mother experienced fever, chills, and severe headache. A blood film sent on the day she gave birth revealed *P. vivax* parasites. The mother recovered completely after treatment with chloroquine and primaquine.

##### Cryptic Malaria

Three cases of cryptic malaria were reported in 2002 and are described in the following case reports:

- **Case 1.** On January 21, 2002, a male aged 56 years from New Jersey was admitted to a local hospital with a 3-week history of fever. He was started on levofloxacin and ceftriaxone for possible pneumonia. On hospital day 2, the laboratory identified *P. falciparum* on a blood film; this result was subsequently confirmed by blood film and polymerase chain reaction (PCR) at CDC. The patient reported no recent history of travel. His last reported trip to a malarious region was to Afghanistan 15 years earlier. He denied any history of blood transfusions or intravenous drug use. He was an obstetrician-gynecologist, and his patient population consisted of immigrants from Africa. He denied any knowledge of needle sticks or cuts on his hands while examining, delivering, or performing surgery on patients with risk factors for malaria. He was successfully treated with quinine, doxycycline, and clindamycin. He made a complete recovery and was discharged.
- **Case 2.** On August 23, 2002, a person aged 19 years from Virginia was examined at a family health clinic; the patient had a 4-day history of fatigue, fever, chills, muscle aches, and sinus pain. Her illness was diagnosed as a sinus infection, and she was treated with azithromycin and desloratadine. Four days later, the patient returned to the clinic with persistent symptoms and also had dizziness and nausea. On physical examination, the patient had fever (temperature: 103.5°F) and tachycardia. Laboratory findings included pancytopenia (platelet count: 61,000 mm<sup>3</sup>; hemoglobin: 10g/dL; and white blood cell count: 3,300/μL). The patient's therapy was changed to levofloxacin. Malaria parasites were identified on a routine complete blood count; a review of the blood film by a local university hospital confirmed the diagnosis of *P. vivax* malaria. The patient had no risk factors for malaria, including international travel, blood transfusion, organ transplantation or needle sharing. The patient recovered after treatment with chloroquine and primaquine (10).
- **Case 3.** On August 25, 2002, a person aged 15 years from Virginia was examined at a local emergency department; the patient had a 2-week history of headaches and 4 days of fever, nausea, vomiting, malaise, and nose bleeds. The patient did not have a history of travel, blood transfusion, organ transplantation, or needle sharing. On physical examination, the patient had a temperature of 105°F, tachycardia, splenomegaly, and jaundice. Laboratory studies revealed pancytopenia (platelet count: 48,000 mm<sup>3</sup>; hemoglobin: 11.6 mg/dL; and white blood cell count: 3,200/μL). A malaria film revealed *Plasmodium* species, initially diagnosed as nonfalciparum. The patient was admitted to the hospital and treated with quinine and clindamycin. The blood film results were subsequently confirmed as *P. vivax* by the Virginia Department of Health. The patient experienced tinnitus, requiring discontinuation of the quinine, and subsequently completed treatment with chloroquine and primaquine (10).

These two cases from Northern Virginia were investigated by local public health officials and CDC, who concluded that the cases represented an outbreak of locally acquired mosquito-transmitted malaria. The investigation revealed that the patient aged 19 years often visited friends who lived directly across the street from the home of the patient aged 15 years. PCR was performed on blood from both patients, and it revealed that the infecting parasites were genotypically identical to each other, indicating a common source. Medical charts from two local hospitals were reviewed, and local physicians were contacted; however, no other cases of malaria were identified (10).

### Induced Malaria

One case of induced malaria was reported in 2002 and is described in the following case report:

- **Case 1.** On June 30, 2002, *P. malariae* was diagnosed in a female aged 84 years, who was being regularly transfused with red blood cells for anemia and angiodysplasia. The laboratory result was subsequently confirmed by blood film and PCR at CDC. Ten donors from whom the patient had received packed red blood cells in the previous 4 months were tested, and one was positive for *P. malariae* by serology. The implicated infective donor, a male aged 17 years, had emigrated from West Africa in 1994 and had donated blood in 2002. The patient was transfused with this unit on May 1, 2002. Blood samples from the donor sent to CDC revealed immunofluorescent antibody titers of >1:16384 for *P. malariae*. Parasites were not detected in the donor's blood film nor by PCR testing. Upon subsequent notification and interview, the donor denied ever having had malaria and reported no history indicative of prior malarial infection (personal communication, Monica Parise, M.D., CDC, National Center for Infectious Diseases, January 2004).

### Deaths Attributed to Malaria

Eight deaths attributable to malaria were reported in 2002 and are described in the following case reports:

- **Case 1.** On February 12, 2002, a female aged 33 years, with a history of seizure disorder, was brought by paramedics to a hospital emergency department with respiratory distress. She had a 5-day history of fever, and a 1-day history of lethargy and difficulty breathing. During the course of her illness, she sought care at a clinic on two separate occasions and was discharged with a diagnosis of viral syndrome. Three weeks before the onset of symptoms, the patient had returned from a 2-week missionary trip to Sudan. The patient had been prescribed weekly mefloquine for malaria chemoprophylaxis, but was reported to be noncompliant with the regimen. On triage examination, the patient had tachypnea (respiratory rate: 28 breaths/minute), tachycardia (pulse: 112 beats/minute), cool extremities, and scleral icterus. Before being seen by the physician in the emergency department, the patient suffered a prolonged generalized seizure, which was refractory to anticonvulsant therapy. She experienced respiratory failure and required endotracheal intubation and mechanical ventilation. Soon after intubation, she suffered a cardiac arrest and died. Postmortem examination revealed severe *P. falciparum* infection with diffuse pulmonary edema and hepatosplenomegaly.
- **Case 2.** On April 5, 2002, a male aged 54 years was examined at his primary-care physician's office. The patient had a 1-week history of fever, fatigue, and loose stools. He had been working in Cameroon and Chad for 2 months and had returned



10 days before the visit to his physician. He had not taken malaria chemoprophylaxis. He was treated as an outpatient with metronidazole. During the next 4 days, he experienced weakness with difficulty standing up, anorexia, and dark urine, which lead him to return to his physician. Laboratory examination demonstrated renal insufficiency (blood urea nitrogen: 86 mg/dL; creatinine: 3.1 mg/dL) and thrombocytopenia (14,000/mm<sup>3</sup>). A blood film was taken at the physician's office, and the patient was administered a dose of hydroxychloroquine presumptively, before results of the blood film were available. He was sent to the emergency department and subsequently admitted to the intensive care unit. On physical exam, he appeared ill, with pale conjunctiva, dry mucous membranes, and cool extremities. He was hypotensive (blood pressure: 82/52 mmHg) and tachycardic (heart rate: 125 beats/minute). Repeat laboratory examination in the emergency department demonstrated acidosis (bicarbonate: 15.5 mmol/L), renal insufficiency (creatinine: 3.7 mg/dL), and thrombocytopenia. He was initially continued on hydroxychloroquine. Approximately 10 hours after admission, the blood film revealed ring trophozoites consistent with *P. falciparum* infection. The parasite density was not reported. The patient was started on oral quinine and doxycycline. Approximately 20 hours after admission, the patient experienced a decreased level of consciousness, followed by sudden onset of severe respiratory distress. He was determined to be severely anemic (7.4 g/dL). The patient suffered a cardiac arrest, could not be resuscitated, and died 28 hours after admission.

- **Case 3.** On May 17, 2002, a male aged 43 years was admitted to a local hospital with a 5-day history of fever, chills, joint pain, and anorexia. Six days before admission, he had returned from Uganda, where he had worked as a missionary for 1 month. The patient had not taken malaria chemoprophylaxis. Physical examination revealed fever (temperature: 104.5°F), tachycardia (heart rate: 112 beats/minute), and hypotension (blood pressure: 86/63 mmHg). Initial laboratory findings included thrombocytopenia (platelets: 50,000 mm<sup>3</sup>), prolonged prothrombin time (18.1 seconds), prolonged partial thromboplastin time (52 seconds), elevated total bilirubin (5.7 mg/dL), and elevated hepatic transaminases. A blood film demonstrated intraerythrocytic ring forms consistent with *P. falciparum*. The parasite density was not reported. The patient was started on oral quinine and doxycycline and admitted to the intensive care unit. On hospital day 2, he became afebrile, and his blood pressure stabilized. With his improved condition, he was transferred to the regular in-patient ward. On hospital day 3, he experienced respiratory distress, and a chest radiograph revealed pulmonary edema and bilateral pleural effusions. His illness was diagnosed as adult respiratory distress syndrome, and his antimalarial treatment was changed to intravenous quinidine and doxycycline. He experienced respiratory failure and refractory hypotension on hospital day 4. He was treated with mechanical ventilation and vasopressors. A repeat blood film was negative for *P. falciparum*. On hospital day 5, the patient experienced wide-complex tachycardia during the placement of an internal jugular catheter, requiring treatment with an intravenous lidocaine infusion. The intravenous quinidine was discontinued after a repeat electrocardiogram revealed a prolonged Q-T interval (i.e., the time from electrocardiogram Q wave to the end of the T wave corresponding to electrical systole). He experienced bilateral pneumothoraces and acute renal failure. The patient never regained consciousness and died on hospital day 7.
- **Case 4.** On June 1, 2002, a previously healthy male aged 46 years was asked to return to the emergency department and admitted to the hospital after a blood film, taken 2 days earlier, revealed malaria parasites. He had returned from a 2-week trip to Nigeria 10 days earlier, and he had not taken malaria chemoprophylaxis. During his first visit to the emergency department, the patient complained of fever, fatigue, and chills and was sent home with a diagnosis of probable viral syndrome, before obtaining the results of the blood film. When he returned to the emergency department on June 1, he reported persistent fever and chills, as well as myalgias, night sweats, and anorexia. Physical examination revealed scleral icterus. Laboratory investigations on admission revealed thrombocytopenia (50,000/mm<sup>3</sup>), elevated creatinine (2.7 mg/dL), elevated bilirubin (4.9 mg/dL), and elevated liver transaminases. The laboratory was unable to identify the malaria species and did not report a parasite density. A chest radiograph revealed bilateral patchy infiltrates. The patient was started on oral quinine and doxycycline. On hospital day 2, the patient had persistent high fever and experienced vomiting, worsening renal insufficiency (creatinine: 4.7 mg/dL), worsening anemia with a 3.2-g/dL drop in hemoglobin from admission (from 13.7 g/dL to 10.5 g/dL), and further elevation in bilirubin and liver transaminases. His blood film was reviewed by a pathologist who reported the species *P. falciparum* with >50% parasitemia. The patient underwent exchange transfusion and was treated with intravenous quinidine and doxycycline. During the following 48 hours, he suffered renal failure, pulmonary edema, and congestive heart failure. He required hemodialysis as well as mechanical ventilation for respiratory failure associated with adult respiratory distress syndrome. Repeat blood films on the fourth and fifth day after admission revealed 3% and 1% parasitemia, respectively. After receiving 2 days of oral doxycycline and quinine and 7 days of intravenous doxycycline and quinidine, all antimalarial medication was discontinued. A blood film collected 12 days after admission was negative. His clinical course continued to deteriorate. He experienced disseminated intravascular coagulopathy, and on hospital day 19, he suffered cardiac arrest and died.
- **Case 5.** On June 9, 2002, a female aged 51 years was admitted to a local hospital with a 1-week history of fever, chills, and back pain. Friends, who noted an altered level of consciousness, brought her to the emergency department. She had traveled to Nigeria and Ghana for 3 weeks and returned to the United States approximately 10 days before admission. The patient reportedly had not taken malaria chemoprophylaxis. Examination revealed mild hypotension (blood pressure: 94/50 mmHg), tachycardia (136 beats/minute), and altered mental status. Initial laboratory findings included anemia (hemoglobin: 9.7 g/dL); thrombocytopenia (platelets: 27,000 mm<sup>3</sup>); decreased bicarbonate (15 mmol/L); renal failure (blood urea nitrogen: 138 mg/dL; creatinine: 8.5 mg/dL); elevated total bilirubin (8.1 mg/dL); and elevated hepatic transaminases. A malaria blood film demonstrated *P. falciparum* (parasitemia >10%). She was started on intravenous quinidine and doxycycline and placed on mechanical ventilation in the emergency department. She was admitted to the intensive care unit and received an exchange transfusion shortly after admission. She was treated with vasopressors and started on hemodialysis. On hospital day 3, she experienced pulmonary edema. Despite a repeat blood film on hospital day 3 that revealed <1% parasitemia, her clinical condition continued to deteriorate. She required increasing ventilatory support, remained hypotensive, and experienced disseminated intravascular coagulation. On hospital day 4, she was treated with one cycle of plasmapheresis, which was completed without complication. The patient demonstrated no improvement and died on hospital day 5.
- **Case 6.** On October 4, 2002, a male aged 67 years was admitted to the hospital with a 7-day history of progressive fatigue

with episodes of mental confusion and a 3-day history of fevers, shaking chills, headache, gross hematuria, and nausea. He had returned from a 3-week trip to Zambia 3 days earlier. He had not taken malaria chemoprophylaxis. Initial physical exam was notable for hypotension (blood pressure: 86/58 mmHg), scleral icterus, and hepatosplenomegaly. Laboratory examination revealed hyponatremia (125 mmol/L), elevated total bilirubin (4.2 mg/dL), and thrombocytopenia ( $17,000/\text{mm}^3$ ). A blood film revealed *P. falciparum* (9.2% parasitemia). Treatment with oral quinine and doxycycline was initiated. On hospital day 2, he became obtunded, experienced a right gaze preference, and suffered a focal seizure. A computed axial tomography scan of the head was normal. Repeat laboratory studies revealed persistent hyponatremia, thrombocytopenia, renal insufficiency (blood urea nitrogen: 66 mg/dL; creatinine: 2.2 mg/dL), and acidosis (bicarbonate: 15 mmol/L). His antimalarial therapy was changed to intravenous quinidine and doxycycline. He was treated with mechanical ventilation and vasopressors. On hospital day 3, he experienced acute renal failure, adult respiratory distress syndrome, and severe anemia (hemoglobin: 6.3 g/dL). The parasitemia decreased with treatment, but the patient never regained consciousness and died on hospital day 5.

- **Case 7.** On November 2, 2002, a previously healthy male aged 55 years was transported to a local hospital emergency department after becoming acutely unresponsive at home. He suffered cardiac arrest and died shortly after arrival. He had been working as a missionary in Africa for 6 months and had recently returned to the United States. Whether the patient had taken malaria chemoprophylaxis was unknown. No further details regarding his symptoms were available. Autopsy findings included histopathologic changes in multiple organs consistent with malaria and focal marked atherosclerosis of the coronary arteries. PCR performed on whole blood revealed *P. falciparum* infection. The medical examiner identified the cause of death as atherosclerotic cardiovascular disease with malaria as a contributing factor.
- **Case 8.** On November 19, 2002, a male aged 50 years was found dead at his home. No further details regarding symptoms before his death were available. He had traveled to Sudan and Uganda and had returned two weeks before his death. He had not taken malaria chemoprophylaxis. He was reportedly philosophically opposed to allopathic medicine. He became ill soon after his return to the United States but did not seek care. Postmortem blood films demonstrated a substantial number of trophozoites consistent with *P. falciparum*.

### Discussion

A total of 1,337 cases of malaria were reported to CDC for 2002, representing a 3.3% decrease from the 1,383 cases reported for 2001. This change primarily resulted from a decrease in cases acquired in the Americas. Since 2000, CDC has routinely contacted state health departments to ask for outstanding malaria case reports from the previous reporting year or for a statement that reporting is complete. The decrease in cases in 2002, compared with 2001, probably is a result of expected variation in the number of cases, although other possibilities include decreased international travel, changing patterns of travel (e.g., decreased immigration from malarious areas), or an increased use of effective antimalarial chemoprophylaxis.

One reason for conducting malaria surveillance is to monitor for prophylaxis failures that might indicate emergence of drug resistance; however, approximately 75% of imported malaria among U.S. civilians occurred among persons who were either not taking prophylaxis or were taking nonrecommended prophylaxis for the region to which they were traveling. Of the cases where appropriate prophylaxis was reported and for whom adequate information was available regarding species and onset of symptoms to indicate that the infection was a primary one rather than a relapse, the majority reported noncompliance with recommended regimen or had insufficient information to determine whether these cases represented problems with adherence while using correct antimalarial chemoprophylaxis, malabsorption of the antimalarial drug, or emerging drug resistance. Among patients who reported compliance with a recommended regimen, serum drug levels were only available for one patient. Therefore, differentiating among inaccurate reporting of compliance, malabsorption of the antimalarial drug, and emerging drug resistance is impossible. No conclusive evidence exists to indicate a single national or regional source of infection among this group of patients or the failure of a particular chemoprophylactic regimen. Health-care providers are encouraged to contact CDC rapidly whenever they suspect chemoprophylaxis failure, thus enabling measurement of serum drug levels of the antimalarial drugs in question.

In 2001, to better evaluate chemoprophylaxis failures, CDC revised the NMSS case report form to facilitate collection of more thorough data regarding chemoprophylaxis. The revised form solicits more detailed information regarding the prescribed regimen, the degree of compliance with the regimen, and the reasons for noncompliance, if any. Data gathered from the responses will be useful in generating public health messages to improve use of antimalarial chemoprophylaxis and therefore decrease malaria-associated morbidity and mortality among U.S. civilians.

The importance of taking correct precautions and chemoprophylaxis is underscored by the eight fatal cases of malaria that occurred in the United States in 2002. An earlier review of deaths attributed to malaria in the United States identified specific risk factors for fatal malaria, including failure to take recommended antimalarial chemoprophylaxis, refusal of or delay in seeking medical care, and misdiagnosis (11).

The occurrence of 12 cases of malaria among pregnant U.S. civilians is also cause for concern. Malaria during pregnancy among nonimmune women is more likely to result in severe disease or contribute to an adverse outcome than malaria in nonpregnant women (12); the fetus might be adversely affected as well (13). Pregnant travelers should be counseled to avoid travel to malarious areas, if possible. If deferral of travel is impossible, pregnant women should be informed that the risks for malaria outweigh those associated with prophylaxis and that safe chemoprophylaxis regimens are available. Specific guidance for pregnant travelers is available from CDC's Internet site at [http://www.cdc.gov/travel/mal\\_preg\\_pub.htm](http://www.cdc.gov/travel/mal_preg_pub.htm).

Signs and symptoms of malaria are often nonspecific, but fever is usually present. Other symptoms include headache, chills, increased sweating, back pain, myalgia, diarrhea, nausea, vomiting, and cough. Prompt diagnosis requires that malaria be included in the differential diagnosis of illness in a febrile person with a history of travel to a malarious area. Clinicians should ask all febrile patients for a travel history, including when evaluating febrile illnesses among international visitors, immigrants, refugees, migrant laborers, and international travelers.

Prompt treatment of suspected malaria is essential, because persons with *P. falciparum* infection are at risk for experiencing life-threatening complications soon after the onset of illness. Ideally, therapy for malaria should be initiated immediately after the diagnosis has been confirmed by a positive blood film. Treatment should be determined on the basis of the infecting *Plasmodium* species, the probable geographic origin of the parasite, the parasite density, and the patient's clinical status (14). If the diagnosis of malaria is 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., Central America). Therefore, therapy for presumed *P. falciparum* malaria should usually entail use of a drug effective against such resistant strains.

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 or treatment of patients with suspected or confirmed malaria should call CDC's National Center for Infectious Diseases, Division of Parasitic Diseases, at 770-488-7788 during regular business hours or CDC's Emergency Operations Center, at 770-488-7100 during evenings, weekends, and holidays (ask to page person on call for Malaria Branch). These resources are intended for use by health-care professionals only.

Detailed recommendations for preventing malaria are available to the general public 24 hours/day from CDC by telephone at 877-394-8747 (toll-free voice information system) or 888-232-3299 (toll-free facsimile request line), or on the Internet at <http://www.cdc.gov/travel/diseases.htm#malaria>. In addition, CDC biannually publishes recommendations in *Health Information for International Travel* (commonly referred to as *The Yellow Book*) (10), which is available for purchase from the Public Health Foundation (telephone: 877-252-1200 or 301-645-7773); it is also available and updated more frequently on CDC's Internet site at <http://www.cdc.gov/travel>.

CDC provides technical support for health-care providers in diagnosing malaria through DPDx, a program that enhances diagnosis of parasitic diseases throughout the world. It includes an Internet site, <http://www.dpd.cdc.gov/DPDx/>, that contains information regarding laboratory diagnosis, geographic distribution, clinical features, treatment, and life cycles of >100 different parasite species, including malaria parasites. The DPDx Internet site is also a portal for diagnostic assistance for health-care providers through tediagnosis. Digital images captured from diagnostic specimens can be submitted for diagnostic consultation through electronic mail. Because laboratories can transmit images to CDC and rapidly obtain answers to their inquiries, this system allows efficient diagnosis of difficult cases and rapid dissemination of information. Approximately 46 public health laboratories in 41 states, Puerto Rico, and Guam have, or are in the process of acquiring, the hardware to perform tediagnosis.

### Acknowledgments

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\* To obtain confirmation diagnosis of blood films from questionable cases and to obtain appropriate treatment recommendations, contact either your state or local health department or CDC's National Center for Infectious Diseases, Division of Parasitic Diseases, Malaria Epidemiology Branch at 770-488-7788.

Table 1

TABLE 1. Number of malaria cases\* among U.S. and foreign civilians and U.S. military personnel — United States, 1973-2002

| Year | U.S. military personnel | U.S. civilians | Foreign civilians | Status not recorded <sup>†</sup> | Total |
|------|-------------------------|----------------|-------------------|----------------------------------|-------|
| 1973 | 41                      | 103            | 78                | 0                                | 222   |
| 1974 | 21                      | 158            | 144               | 0                                | 323   |
| 1975 | 17                      | 199            | 232               | 0                                | 448   |
| 1976 | 5                       | 178            | 227               | 5                                | 415   |
| 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 |

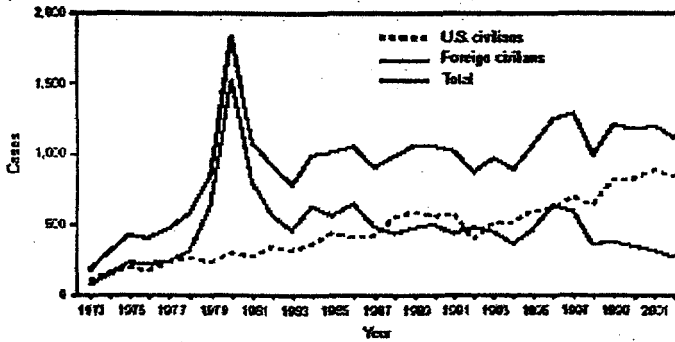
\* A case was defined as symptomatic or asymptomatic illness that occurs in the United States in a person who has microscopy-confirmed malaria parasitemia, regardless of whether the person had previous attacks of malaria while in other countries. A subsequent attack of malaria occurring in a person is counted as an additional case if the demonstrated *Plasmodium* species differs from the initially identified species. A subsequent attack of malaria occurring in a person while in the United States could indicate a relapsing infection or treatment failure resulting from drug resistance if the demonstrated *Plasmodium* species is the same species identified previously.

<sup>†</sup> The increase in persons with unknown civil status that occurred in the 1990s might be attributed to a change in the surveillance form.

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Figure 1

FIGURE 1. Number of malaria cases among U.S. and foreign civilians — United States,\* 1973–2002†



\* Includes Puerto Rico, Guam, and the U.S. Virgin Islands.  
 † The substantial increase in the number of cases reported for 1980 primarily reflects cases diagnosed among immigrants from Southeast Asia.

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Table 2

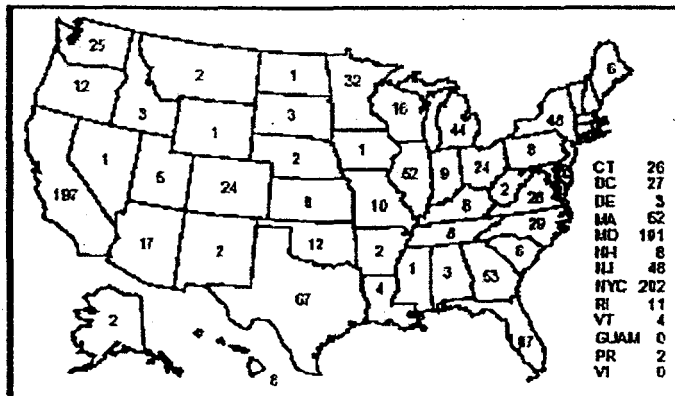
TABLE 2. Number of malaria cases, by *Plasmodium* species — United States, 2000, 2001, and 2002

| <i>Plasmodium</i> species | 2000  |         | 2001  |         | 2002  |         |
|---------------------------|-------|---------|-------|---------|-------|---------|
|                           | No.   | (%)     | No.   | (%)     | No.   | (%)     |
| <i>P. falciparum</i>      | 611   | (43.6)  | 693   | (50.1)  | 699   | (52.3)  |
| <i>P. vivax</i>           | 522   | (37.2)  | 395   | (27.8)  | 339   | (25.4)  |
| <i>P. malariae</i>        | 67    | (4.8)   | 62    | (4.5)   | 38    | (2.8)   |
| <i>P. ovale</i>           | 32    | (2.3)   | 50    | (3.6)   | 37    | (2.8)   |
| Mixed                     | 9     | (0.6)   | 14    | (1.0)   | 11    | (0.8)   |
| Undetermined              | 161   | (11.5)  | 179   | (12.9)  | 213   | (15.9)  |
| Total                     | 1,402 | (100.0) | 1,383 | (100.0) | 1,337 | (100.0) |

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Figure 2

FIGURE 2. Number of malaria cases, by state in which the disease was diagnosed — United States, 2002



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Table 3

TABLE 3. Imported malaria cases, by country of acquisition and *Plasmodium* species — United States, 2002

| Country of acquisition      | <i>Plasmodium</i> species |                 |                    |                 |         |       | Total |
|-----------------------------|---------------------------|-----------------|--------------------|-----------------|---------|-------|-------|
|                             | <i>P. falciparum</i>      | <i>P. vivax</i> | <i>P. malariae</i> | <i>P. ovale</i> | Unknown | Mixed |       |
| Africa                      | 613                       | 71              | 30                 | 30              | 153     | 6     | 903   |
| Benin                       | 2                         | 0               | 0                  | 0               | 1       | 0     | 3     |
| Burkina Faso                | 7                         | 0               | 0                  | 0               | 2       | 0     | 9     |
| Burundi                     | 0                         | 0               | 1                  | 0               | 0       | 0     | 1     |
| Cameroon                    | 27                        | 5               | 1                  | 5               | 9       | 0     | 47    |
| Central African Republic    | 6                         | 0               | 0                  | 0               | 0       | 0     | 6     |
| Chad                        | 0                         | 0               | 1                  | 0               | 3       | 0     | 4     |
| Congo                       | 4                         | 1               | 0                  | 1               | 4       | 0     | 10    |
| Cote d'Ivoire               | 28                        | 4               | 1                  | 1               | 4       | 1     | 39    |
| Equatorial Guinea           | 1                         | 0               | 0                  | 0               | 0       | 0     | 1     |
| Eritrea                     | 0                         | 1               | 0                  | 0               | 0       | 0     | 1     |
| Ethiopia                    | 3                         | 10              | 0                  | 1               | 2       | 0     | 16    |
| Gabon                       | 1                         | 0               | 0                  | 0               | 2       | 0     | 3     |
| Gambia                      | 5                         | 2               | 0                  | 0               | 1       | 0     | 8     |
| Ghana                       | 104                       | 6               | 4                  | 3               | 19      | 2     | 138   |
| Guinea                      | 8                         | 1               | 0                  | 0               | 1       | 0     | 10    |
| Kenya                       | 33                        | 6               | 2                  | 2               | 9       | 0     | 52    |
| Liberia                     | 28                        | 3               | 2                  | 0               | 6       | 0     | 39    |
| Madagascar                  | 2                         | 1               | 0                  | 0               | 1       | 0     | 4     |
| Malawi                      | 5                         | 0               | 1                  | 1               | 1       | 0     | 8     |
| Mali                        | 12                        | 0               | 0                  | 0               | 0       | 0     | 12    |
| Mauritania                  | 0                         | 1               | 0                  | 0               | 0       | 1     | 2     |
| Mozambique                  | 1                         | 1               | 0                  | 0               | 0       | 0     | 2     |
| Niger                       | 1                         | 2               | 0                  | 0               | 0       | 0     | 3     |
| Nigeria                     | 225                       | 9               | 10                 | 6               | 57      | 2     | 309   |
| Rwanda                      | 1                         | 0               | 0                  | 0               | 0       | 0     | 1     |
| Senegal                     | 17                        | 2               | 1                  | 0               | 0       | 0     | 20    |
| Sierra Leone                | 15                        | 1               | 0                  | 0               | 1       | 0     | 17    |
| Somalia                     | 2                         | 0               | 0                  | 0               | 0       | 0     | 2     |
| South Africa                | 4                         | 1               | 1                  | 0               | 0       | 0     | 6     |
| Sudan                       | 2                         | 2               | 0                  | 2               | 0       | 0     | 6     |
| Tanzania                    | 4                         | 3               | 0                  | 0               | 3       | 0     | 10    |
| Togo                        | 5                         | 0               | 0                  | 0               | 2       | 0     | 7     |
| Tunisia                     | 0                         | 0               | 0                  | 0               | 1       | 0     | 1     |
| Uganda                      | 15                        | 3               | 1                  | 3               | 8       | 0     | 30    |
| Zaire                       | 0                         | 0               | 1                  | 0               | 1       | 0     | 2     |
| Zambia                      | 8                         | 0               | 0                  | 2               | 3       | 0     | 13    |
| Zimbabwe                    | 2                         | 0               | 1                  | 0               | 0       | 0     | 3     |
| West Africa, unspecified    | 12                        | 0               | 0                  | 1               | 2       | 0     | 15    |
| Central Africa, unspecified | 1                         | 0               | 0                  | 0               | 0       | 0     | 1     |
| East Africa, unspecified    | 0                         | 3               | 0                  | 0               | 0       | 0     | 3     |
| Africa, unspecified         | 22                        | 3               | 2                  | 2               | 10      | 0     | 39    |
| Asia                        | 18                        | 130             | 3                  | 3               | 14      | 3     | 171   |
| Afghanistan                 | 0                         | 2               | 0                  | 0               | 0       | 0     | 2     |
| Burma (Myanmar)             | 0                         | 3               | 0                  | 0               | 0       | 0     | 3     |
| China                       | 0                         | 2               | 0                  | 0               | 0       | 0     | 2     |
| India                       | 5                         | 72              | 2                  | 1               | 10      | 0     | 90    |
| Indonesia                   | 1                         | 13              | 0                  | 1               | 1       | 0     | 16    |
| Iraq                        | 1                         | 0               | 0                  | 0               | 0       | 0     | 1     |
| Korea (South)               | 0                         | 21              | 0                  | 0               | 2       | 0     | 23    |
| Leo PDR                     | 2                         | 1               | 0                  | 0               | 0       | 0     | 3     |
| Pakistan                    | 0                         | 10              | 0                  | 1               | 0       | 2     | 13    |
| Philippines                 | 3                         | 2               | 1                  | 0               | 1       | 0     | 7     |
| Thailand                    | 3                         | 1               | 0                  | 0               | 0       | 0     | 4     |
| United Arab Emirates        | 0                         | 0               | 0                  | 0               | 0       | 1     | 1     |
| Vietnam                     | 0                         | 1               | 0                  | 0               | 0       | 0     | 1     |
| Yemen                       | 2                         | 0               | 0                  | 0               | 0       | 0     | 2     |
| Asia, unspecified           | 0                         | 1               | 0                  | 0               | 0       | 0     | 1     |
| Southeast Asia, unspecified | 1                         | 1               | 0                  | 0               | 0       | 0     | 2     |

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Table 4.

**TABLE 4. Number of imported malaria cases, by interval between date of arrival in the country and onset of illness and *Plasmodium* species\* — United States, 2002**

| Interval (days) | <i>P. falciparum</i> |         | <i>P. vivax</i> |         | <i>P. malariae</i> |         | <i>P. ovale</i> |         | Mixed |         | Total |         |
|-----------------|----------------------|---------|-----------------|---------|--------------------|---------|-----------------|---------|-------|---------|-------|---------|
|                 | No.                  | (%)     | No.             | (%)     | No.                | (%)     | No.             | (%)     | No.   | (%)     | No.   | (%)     |
| <0†             | 73                   | (15.1)  | 13              | (8.4)   | 3                  | (15.0)  | 2               | (11.1)  | 1     | (16.7)  | 92    | (13.5)  |
| 0-29            | 385                  | (80.0)  | 57              | (36.6)  | 12                 | (60.0)  | 4               | (22.2)  | 3     | (50.0)  | 461   | (67.7)  |
| 30-89           | 19                   | (3.9)   | 35              | (22.6)  | 3                  | (15.0)  | 3               | (16.7)  | 0     | 0       | 60    | (8.8)   |
| 90-179          | 1                    | (0.2)   | 23              | (14.8)  | 1                  | (5.0)   | 6               | (33.3)  | 1     | (16.7)  | 32    | (4.7)   |
| 180-364         | 1                    | (0.2)   | 24              | (15.5)  | 0                  | 0       | 3               | (16.7)  | 1     | (16.7)  | 29    | (4.3)   |
| ≥365            | 3                    | (0.6)   | 3               | (1.9)   | 1                  | (5.0)   | 0               | 0       | 0     | 0       | 7     | (1.0)   |
| Total           | 482                  | (100.0) | 155             | (100.0) | 20                 | (100.0) | 18              | (100.0) | 6     | (100.0) | 681   | (100.0) |

\* Persons for whom *Plasmodium* species, date of arrival in the United States, or date of onset of illness is unknown are not included.

† Persons in these cases in this row are those with onset of illness before arriving in the United States.

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Table 5

**TABLE 5. Number of imported malaria cases among U.S. and foreign civilians, by region of acquisition — United States, 2002\***

| Area or region                    | United States |         | Foreign |         | Total |         |
|-----------------------------------|---------------|---------|---------|---------|-------|---------|
|                                   | No.           | (%)     | No.     | (%)     | No.   | (%)     |
| Africa                            | 641           | (75.5)  | 180     | (66.9)  | 821   | (73.2)  |
| Asia                              | 89            | (10.5)  | 45      | (16.9)  | 134   | (12.0)  |
| Central America and the Caribbean | 57            | (6.7)   | 29      | (10.2)  | 86    | (7.7)   |
| South America                     | 23            | (2.7)   | 8       | (3.0)   | 31    | (2.8)   |
| North America                     | 3             | (0.4)   | 6       | (1.9)   | 9     | (0.8)   |
| Oceania                           | 32            | (3.8)   | 3       | (1.1)   | 35    | (3.1)   |
| Europe/Newly Independent States   | 0             | (0)     | 0       | (0)     | 0     | (0)     |
| Unknown†                          | 4             | (0.4)   | 1       | (0.3)   | 5     | (0.4)   |
| Total                             | 849           | (100.0) | 272     | (100.0) | 1,121 | (100.0) |

\* Persons for whom U.S. or foreign status is not known are excluded.

† Region of acquisition is unknown.

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Table 6

**TABLE 6. Number of imported malaria cases among U.S. civilians, by purpose of travel at the time of acquisition — United States, 2002**

| Category                   | Imported cases |         |
|----------------------------|----------------|---------|
|                            | No.            | (%)     |
| Visiting friends/relatives | 382            | (45.0)  |
| Tourism                    | 87             | (10.2)  |
| Missionary or dependent    | 90             | (10.6)  |
| Business representative    | 65             | (7.7)   |
| Student/teacher            | 52             | (6.1)   |
| Peace Corps volunteer      | 9              | (1.0)   |
| Refugee/immigrant          | 2              | (0.3)   |
| Air crew/sailor            | 2              | (0.3)   |
| Other/mixed purpose        | 56             | (6.6)   |
| Unknown                    | 104            | (12.2)  |
| Total                      | 849            | (100.0) |

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Table 7

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 voice information system  | 24 hours/day  | 877-394-8747 (877-FYI-TRIP)   |
| Prophylaxis         | CDC's Traveler's Health fascimile information service   | 24 hours/day  | 888-232-3299  |
| Prophylaxis         | CDC's Traveler's Health internet site (includes online access to <i>Health Information for International Travel</i> ) | 24 hours/day  | <a href="http://www.cdc.gov/travel">http://www.cdc.gov/travel</a>   |
| Prophylaxis         | <i>Health Information for International Travel (The Yellow Book)</i>  | Order from Public Health Publication Sales<br>P.O. Box 753<br>Waldorf, MD 20604 | 877-252-1200 or<br>301-645-7773 or<br><a href="http://www.phf.org">http://www.phf.org</a>   |
| Diagnosis           | CDC's Division of Parasitic Diseases diagnostic internet site (DPDx)  | 24 hours/day  | <a href="http://www.dpd.cdc.gov/dpdx">http://www.dpd.cdc.gov/dpdx</a>   |
| Diagnosis           | CDC's Division of Parasitic Diseases diagnostic CD-ROM (DPDx)   | Order by electronic mail from CDC<br>Division of Parasitic Diseases             | <a href="mailto:dpdx@cdc.gov">dpdx@cdc.gov</a>  |
| Treatment*          | CDC's Malaria Branch  | 8:00 am-4:30 pm Eastern Time,<br>Monday-Friday                                  | 770-488-7788*   |
| Treatment           | CDC's Malaria Branch  | 4:30 pm-8:00 am Eastern Time,<br>evenings, weekends, and holidays               | 770-488-7100* (This is the number for the CDC's<br>Emergency Operations Center. Ask staff member<br>to page person on call for Malaria Branch). |

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

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