Surveillance for Chronic Fatigue Syndrome — Four U.S. Cities, September 1989 Through August 1993

Tetanus Surveillance — United States, 1991–1994

Malaria Surveillance — United States, 1993

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*Abbreviations

ATSDR	Agency for Toxic Substances and Disease Registry
CIO	Centers/Institute/Offices
EPO	Epidemiology Program Office
IHPO	International Health Program Office
NCCDPHP	National Center for Chronic Disease Prevention and Health Promotion
NCEH	National Center for Environmental Health
NCEHIC	National Center for Environmental Health and Injury Control
NCID	National Center for Infectious Diseases
NCIPC	National Center for Injury Prevention and Control
NCPS	National Center for Prevention Services
NIOSH	National Institute for Occupational Safety and Health
NIP	National Immunization Program

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Neisseria gonorrhoeae, Antimicrobial Resistance in	NCPS	1993; Vol. 42, No. SS-3
Neural Tube Defects	NCEH	1995; Vol. 44, No. SS-4
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Sudden Unexplained Death Syndrome Among Southeast Asian Refugees	NCEHIC, NCPS	1987; Vol. 36, No. 1SS
Suicides, Persons 15–24 Years of Age	NCEHIC	1988; Vol. 37, No. SS-1
Syphilis, Congenital	NCPS	1993; Vol. 42, No. SS-6
Syphilis, Primary & Secondary	NCPS	1993; Vol. 42, No. SS-3
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Surveillance for Chronic Fatigue Syndrome — Four U.S. Cities, September 1989 Through August 1993

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Abstract

Problem/Condition: Although chronic fatigue syndrome (CFS) has been recognized as a cause of morbidity in the United States, the etiology of CFS is unknown. In addition, information is incomplete concerning the clinical spectrum and prevalence of CFS in the United States.

Reporting Period Covered: This report summarizes CFS surveillance data collected in four U.S. cities from September 1989 through August 1993.

Description of System: A physician-based surveillance system for CFS was established in four U.S. metropolitan areas: Atlanta, Georgia; Wichita, Kansas; Grand Rapids, Michigan; and Reno, Nevada. The objectives of this surveillance system were to collect descriptive epidemiologic information from patients who had unexplained chronic fatigue, estimate the prevalence and incidence of CFS in defined populations, and describe the clinical course of CFS. Patients aged ≥18 years who had had unexplained, debilitating fatigue or chronic unwellness for at least 6 months were referred by their physicians to a designated health professional(s) in their area. Those patients who participated in the surveillance system a) were interviewed by the health professional(s); b) completed a self-administered questionnaire that included their demographic information, medical history, and responses to the Beck Depression Inventory, the Diagnostic Interview Schedule, and the Sickness Impact Profile; c) submitted blood and urine samples for laboratory testing; and d) agreed to a review of their medical records. On the basis of this information, patients were assigned to one of four groups: those whose illnesses met the criteria of the 1988 CFS case definition (Group I); those whose fatigue or symptoms did not meet the criteria for CFS (Group II); those who had had an identifiable psychological disorder before onset of fatigue (Group III); and those who had evidence of other medical conditions that could

have caused fatigue (Group IV). Patients assigned to Group III were further evaluated to determine the group to which they would have been assigned had psychological illness not been present. The epidemiologic characteristics of the illness and the frequency of symptoms among patients were evaluated, and the prevalence and incidence of CFS were estimated for each of the areas.

Results: Of the 648 patients referred to the CFS surveillance system, 565 (87%) agreed to participate. Of these, 130 (23%) were assigned to Group I; 99 (18%), Group II; 235 (42%), Group III; and 101 (18%), Group IV. Of the 130 CFS patients, 125 (96%) were white and 111 (85%) were women. The mean age of CFS patients at the onset of illness was 30 years, and the mean duration of illness at the time of the interview was 6.7 years. Most (96%) CFS patients had completed high school, and 38% had graduated from college. The median annual household income for CFS patients was $40,000. In the four cities, the age-, sex-, and race-adjusted prevalences of CFS for the 4-year surveillance period ranged from 4.0 to 8.7 per 100,000 population. The age-adjusted 4-year prevalences of CFS among white women ranged from 8.8 to 19.5 per 100,000 population.

Interpretation: The results of this surveillance system were similar to those in previously published reports of CFS. Additional studies should be directed toward determining whether the data collected in this surveillance system were subject to selection bias (e.g., education and income levels might have influenced usage of the health-care system, and the populations of these four surveillance sites might not be representative of the U.S. population).

Actions Taken: In February 1997, CDC began a large-scale, cross-sectional study at one surveillance site (Wichita) to describe more completely the magnitude and epidemiology of unexplained chronic fatigue and CFS.

INTRODUCTION

Although chronic fatigue syndrome (CFS) has been recognized as a cause of morbidity in the United States, the etiology of the syndrome is unknown, and only symptomatic treatments are available. No biologic markers of CFS have been identified, and no diagnostic tests have been developed; the illness is diagnosed primarily on the basis of symptoms and signs reported by the patient and exclusion of other possible causes of prolonged, debilitating fatigue.

Information is incomplete concerning the characteristics of patients who have unexplained fatigue, their symptoms, and the prevalence of chronic fatigue. Fatigue is a common complaint, and chronic fatigue is a well-known symptom of many physical and psychological illnesses (*1,2*). CFS patients constitute a subgroup of persons who have chronic fatigue.

Outbreaks of similar illnesses were described before the early 1980s (*3*), when interest in endemic CFS was heightened (*4*). Several early reports suggested an association between the symptoms and Epstein-Barr virus (EBV), and the illness was referred to as "chronic EBV syndrome" (*4–6*). Subsequent studies indicated that CFS patients were no more likely than non-CFS patients to have evidence of infection with EBV (*7*).

In 1988, a CFS case definition was published for the purpose of improving comparability across research studies (*8*). According to this definition, other clinical

conditions that might have caused the fatigue must have been excluded. At least six of the following 11 symptoms must have begun at or after the onset of illness and must have persisted or recurred for at least 6 months: mild fever (37.5–38.6 C [99.5–101.5 F]) (as measured by the patient) and/or chills; sore throat; painful lymph nodes; muscular discomfort or myalgia; prolonged (≥24 hours) generalized fatigue after exercise that would have been easily tolerated before the illness; generalized headaches different from those the patient had before the onset of illness; migratory arthralgia without joint swelling or redness; neuropsychologic complaints (e.g., photophobia, transient visual scotomata, forgetfulness, excessive irritability, confusion, difficulty thinking, inability to concentrate, and depression); sleep disturbance; sudden onset of symptoms*; and unexplained generalized muscle weakness. Furthermore, unless eight or more of these symptoms have been present, at least two of the following three physical signs must have been documented by a physician on at least two occasions and at least 1 month apart: low-grade fever (37.6–38.6 C [99.6–101.5 F]), nonexudative pharyngitis, and palpable or tender lymph nodes.

Only two peer-reviewed studies have made population-based estimates of the prevalence of a chronic fatiguing illness. The first study, which was conducted in Australia, relied on solicitation of medical-practitioner referrals to identify persons who had had at least 6 months of unexplained prolonged fatigue accompanied by neuropsychiatric dysfunction (9). Using this definition, the researchers estimated the prevalence as 37 cases per 100,000 population. The second study, which was conducted in the United States, was based on data from a nationwide population-based mental health survey of 13,000 persons (10). This latter study used information obtained by administering the Diagnostic Interview Schedule (DIS) (11) to approximate the CFS case definition. Only one case of CFS was identified, for an estimated prevalence of 7.4 cases per 100,000 population.

From September 1989 through August 1993, CDC conducted physician-based surveillance for unexplained chronic fatigue in Atlanta, Georgia; Wichita, Kansas; Grand Rapids, Michigan; and Reno, Nevada. The primary objectives of this system were to a) collect descriptive epidemiologic information from patients who had unexplained chronic fatigue, b) estimate the prevalence and incidence of CFS in defined populations, and c) describe the clinical course of CFS. This report addresses the first two objectives.

METHODS

Surveillance Sites

Each of the four surveillance sites comprised a central city and its surrounding counties (12). Wichita and Grand Rapids were chosen because they are cities with stable populations whose overall demographic characteristics approximated those of the total U.S. population. Reno was selected because of its close proximity to Incline Village, the site of a 1986 cluster of CFS cases (4). Atlanta was chosen because of the proximity to CDC for special laboratory studies.

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*This factor is not a symptom, but it is considered to be of equal importance as the symptoms for the purposes of the CFS case definition (8).

Surveillance System Procedures

At each surveillance site, physicians whose clientele were likely to include patients who have CFS (i.e., family practitioners, internists, infectious disease specialists, and rheumatologists) were identified by using telephone and medical directories. Of the eligible physicians, 879 were asked to participate in the study; 409 (47%) of these physicians agreed to participate. The site-specific participation rates were 55% in both Wichita and Reno, 45% in Grand Rapids, and 37% in Atlanta (12). The participating physicians were contacted annually to confirm their continued participation and were sent periodic newsletters to inform them of the status of the surveillance system.

Two surveillance nurses were designated in each of the four cities. Patients who possibly had CFS were referred by the participating physicians to the surveillance nurses based in that city. Physicians were asked to refer patients aged ≥18 years who had had at least 6 months of unexplained debilitating fatigue or chronic unwellness. Debilitating fatigue was defined as the patient's subjective report of reduced activity level and greater effort required to perform the same routine activities as were performed before onset of fatigue. Chronic unwellness was defined as a patient's report of two or more of the following symptoms occurring at least monthly: fever, sore throat, unusual muscle weakness, unusual fatigue after exercise, tender lymph nodes, myalgia, and arthralgia.

Those patients who participated in the surveillance system a) were interviewed by at least one of the surveillance nurses in their city, b) completed a self-administered questionnaire, c) submitted blood and urine samples for laboratory testing, and d) agreed to a review of their medical records. The self-administered questionnaire included the patient's demographic information (i.e., self-reported age, race/ethnicity, sex, household income, and educational level), medical history, and responses to the Beck Depression Inventory (BDI) (13) (i.e., to measure the symptoms of depression) and the Sickness Impact Profile (SIP) (14) (i.e., to measure the effects of fatiguing illness on daily activities, attitudes, and behaviors).

During the personal interview, the surveillance nurse(s) obtained informed consent from each participant; reviewed the self-administered questionnaire with the patient; and obtained information concerning the onset, frequency, and severity of all symptoms reported by the patient, including symptoms not included in the CFS case definition, self-reported energy levels, and ability to perform everyday activities. Cognitive function was measured by tests of memory, attention, and concentration. The DIS (11) was administered to identify those patients who had psychological illnesses. Only the DIS sections concerning somatization, panic disorder, generalized anxiety disorder, and depression were used.

For each patient, a battery of standard blood and urine tests was performed, including a complete blood count, urinalysis, and renal analyses and measurements of erythrocyte sedimentation rate, thyroid function, and liver function. The surveillance nurses reviewed for each patient the medical records maintained by the referring physician and summarized the information regarding the symptoms suggestive of CFS, the laboratory test results, other illnesses and health problems, and hospitalizations.

Classification of Participating Patients

A physician review committee (PRC), composed of clinicians and researchers, was established for the purpose of classifying the participating patients into one of four groups (Figure 1). The assignment of each patient into one of these groups was decided by at least three members of the PRC and was based on an independent review of the summarized information for each patient. The PRC reviewers unanimously agreed on the initial classification of 82% of all cases reviewed. When the initial classification was not unanimous, PRC members conferred and reached a consensus. CDC then compiled and analyzed the data for each group of patients.

The 1988 case definition of CFS (*8*) was used as the basis for classification of patients. Patients whose illnesses met the criteria of the CFS case definition (i.e., the CFS patients) were assigned to Group I. Patients whose fatigue or symptoms did not meet the criteria for CFS were assigned to Group II. Patients who had evidence of a psychological disorder that was diagnosable before the onset of fatigue and that could have explained the fatiguing illness were assigned to Group III. Patients in this group were further evaluated to determine the group to which they would have been assigned had psychological illness not been present (i.e., Groups III-I, III-II, or III-IV). Patients who had evidence of a medical condition that could have caused fatigue were assigned to Group IV.

RESULTS

Patients

During the 4-year surveillance period from September 1989 through August 1993, participating physicians referred 648 patients who had had unexplained debilitating fatigue or chronic unwellness for at least 6 months. Of these, 565 (87%) patients agreed to participate in the surveillance system, and 83 (13%) declined. The largest percentage of participants was from Atlanta (46%), followed by Wichita (22%), Reno (18%), and Grand Rapids (14%) (Table 1).

Characteristics and Classification of Participants

Of the 565 patients, 130 (23%) were assigned to Group I; 99 (18%), Group II; 235 (42%), Group III; and 101 (18%), Group IV (Table 1). The distribution of patients by group was similar for all four surveillance sites. The demographic characteristics of patients did not differ significantly by group (Table 2). Most Group I patients were white (96%) and female (85%) and had a median of 14 years of education and a median annual household income of $40,000. The mean age at onset of fatigue for Group I patients was 30 years (range: 15–56 years), and the mean age at the time of the interview was 37 years, resulting in a mean illness duration of 6.7 years.

Symptoms and Signs

Each symptom and sign listed in the CFS case definition was evaluated to determine the frequency with which it was reported by patients. Each symptom was reported by at least 73% of the 130 Group I patients. However, only 48 (37%) Group I

FIGURE1. Use of the 1988 case definition for chronic fatigue syndrome (CFS) to classify participants in the CFS surveillance system, by diagnostic category — four U.S. cities,* September 1989 through August 1993

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┌──────────────────────────────────────────────────────────────┐
│          Participants in CFS surveillance system              │
│  at least 6 months of unexplained fatigue or chronic unwellness│
│                        (n=565)                                 │
└──────────────────────────────────────────────────────────────┘
                              ↓
          ┌──────────────────────────────┐  YES
          │      Psychiatric exclusion    │──────────────→
          │  psychological disorder before │
          │     onset of fatiguing illness │
          └──────────────────────────────┘
                              ↓
          ┌──────────────────────────────┐  YES
          │       Medical exclusion        │──────────→
          │  possible medical explanation  │
          │          for fatigue           │
          └──────────────────────────────┘
                              ↓
   NO     ┌──────────────────────────────┐
  ←───────│           Fatigue             │
          │    not resolved by bedrest;    │
          │   reduces activity at least 50%│
          └──────────────────────────────┘
                              ↓
          ┌──────────────────────────────┐
          │       Symptoms and signs       │
          │      at least six symptoms     │
   NO     │  fever/chills, neurocognitive  │
  ←───────│  complaints, sore throat,      │
          │  headache, arthralgia, myalgia,│
          │  swollen lymph nodes, sleep    │
          │  disturbance, muscle weakness, │
          │  unusual fatigue, or sudden onset│
          │     plus at least two signs    │
          │  palpable lymph nodes,         │
          │  nonexudative pharyngitis,     │
          │  or fever                      │
          │   or two more symptoms         │
          └──────────────────────────────┘
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Group II	Group I	Group IV	Group III
patients whose fatigue or symptoms do not meet CFS criteria (n=99)	patients who have CFS (n=130)	patients whose illness has a possible medical etiology (n=101)	patients who had a psychological disorder before onset of fatigue (n=235)

*Atlanta, Georgia; Wichita, Kansas; Reno, Nevada; and Grand Rapids, Michigan.

patients reported that the onset of their symptoms occurred suddenly (i.e., in <24 hours) (Table 3), and only seven (5%) Group I patients were classified as such on the basis of this criterion in combination with other symptoms and signs. In addition, ≤32% of Group I patients had documented physical criteria that met the CFS case definition.

Symptoms and signs were reported least frequently by Group II patients, although this directly reflected the definition for assignment to this group. Persons who had psychological or medical conditions that possibly explained the fatigue (Groups III and IV, respectively) reported having had more symptoms and signs of CFS than patients in Group II, but fewer symptoms and signs than patients in Group I. Patients assigned to Groups III-I, III-II, and III-IV reported frequencies of symptoms remarkably similar to those of patients in Groups I, II, and IV, respectively.

Symptoms not included in the CFS case definition that were reported by patients included shortness of breath, cough, wheezing, nausea, vomiting, constipation, diarrhea, stomach ache, bloating, ringing in the ears, numbness, poor balance, anger, anxiousness, nightmares, night sweats, chest pain, heart palpitations, itchiness, and skin rashes. No one symptom or group of symptoms was reported by >50% of respondents. Group I patients most often reported symptoms not included in the case definition, followed by patients in Groups III and IV; patients in Group II reported such symptoms least often.

Prevalence

On the basis of 1990 U.S. census data for the counties encompassing each study site, the crude 4-year period prevalence of CFS among persons aged ≥18 years ranged from 3.8 cases per 100,000 population in Atlanta to 9.6 per 100,000 in Wichita, with an overall crude rate of 5.2 per 100,000 (Table 4). The differences in prevalence between the surveillance sites remained after directly adjusting for age, sex, and race.

Because most patients who had CFS were white (98%) and female (85%), the site-specific period prevalences were calculated for this group. For white women, the

TABLE 1. Distribution of patients* participating in the chronic fatigue syndrome (CFS) surveillance system, by diagnostic category[†] — four U.S. cities, September 1989 through August 1993

	Diagnostic category								Total no.
	Group I		Group II		Group III		Group IV		
City	No.	%	No.	%	No.	%	No.	%	
Atlanta, GA	61	(23.6)	48	(18.5)	101	(39.0)	49	(18.9)	259
Grand Rapids, MI	22	(27.5)	12	(15.0)	36	(45.0)	10	(12.5)	80
Reno, NV	19	(19.0)	17	(17.0)	48	(48.0)	16	(16.0)	100
Wichita, KS	28	(22.2)	22	(17.5)	50	(39.7)	26	(20.6)	126
Total	**130**	**(23.0)**	**99**	**(17.5)**	**235**	**(41.6)**	**101**	**(17.9)**	**565**

*Persons aged ≥18 years.
[†]Patients were assigned to one of four groups: those whose illnesses met the criteria of the 1988 CFS case definition (Group I); those whose fatigue or symptoms did not meet the criteria for CFS (Group II); those who had had an identifiable psychological disorder before onset of fatigue (Group III); and those who had evidence of a medical condition that could have caused fatigue (Group IV).

crude prevalence rates ranged from 8.6 cases per 100,000 population in Atlanta to 17.7 per 100,000 in Wichita, with an overall crude rate of 10.8 per 100,000 (Table 4). The overall crude prevalence rate for white men was 2.1 per 100,000. Estimates of site-specific prevalence rates for persons of other racial/ethnic groups were not calculated because of the small number of cases.

The estimated prevalence of unexplained chronic fatigue was based on the 393 patients who did not have evidence of a medical condition that could have caused fatigue (i.e., patients in Groups I and II and patients in Group III who did not have a medical exclusion). The crude period prevalence of chronic fatigue ranged from 12.9 per 100,000 population in Atlanta to 34.3 per 100,000 in Wichita, with an overall

TABLE 2. Demographic characteristics of patients* participating in the chronic fatigue syndrome (CFS) surveillance system, by diagnostic category[†] — four U.S. cities,[§] September 1989 through August 1993

| | Diagnostic category | | | | | | | | | |
| | Group I (n=130) | | Group II (n=99) | | Group III (n=235) | | Group IV (n=101) | | Total | |
Characteristic	No.	%	No.	%	No.	%	No.	%	No.	%
Sex										
Female	111	(85)	77	(78)	193	(82)	78	(77)	459	(81)
Male	19	(15)	22	(12)	42	(18)	23	(13)	106	(19)
Race										
White	125	(96)	97	(99)	222	(94)	93	(95)	537	(97)
Other	5	(2)	2	(1)	13	(6)	18	(5)	28	(3)
Level of education										
Less than high school diploma	3	(2)	5	(5)	9	(4)	3	(3)	20	(4)
High school diploma	18	(14)	10	(10)	30	(13)	15	(15)	73	(13)
Some college and/or technical school	59	(45)	40	(41)	101	(45)	39	(39	239	(44)
College degree or greater	50	(38)	43	(44)	83	(37)	41	(41)	217	(40)
Annual household income										
<$20,000	23	(15)	9	(9)	52	(22)	12	(12)	96	(17)
$20,000–$50,000	55	(42)	48	(48)	103	(44)	46	(46)	252	(45)
>$50,000	42	(32)	37	(37)	57	(24)	37	(37)	173	(31)
Mean age at onset of fatigue (yrs)	30		32		35		38		34	
Mean age at time of interview (yrs)	37		38		41		44		40	
Mean duration of illness (yrs)	6.7		6.3		5.8		5.8		6.1	

*Persons aged ≥18 years.
[†]Totals may not add up to 100% because of differences in response rates. Patients were assigned to one of four groups: those whose illnesses met the criteria of the 1988 CFS case definition (Group I); those whose fatigue or symptoms did not meet the criteria for CFS (Group II); those who had had an identifiable psychological disorder before onset of fatigue (Group III); and those who had evidence of a medical condition that could have caused fatigue (Group IV).
[§]Atlanta, Georgia; Wichita, Kansas; Grand Rapids, Michigan; and Reno, Nevada.

rate of 18.4 per 100,000 (Table 5). As with the CFS prevalence differences among sites, the differences in prevalence of chronic fatigue remained after adjustment, using 1990 U.S. census data, for sex, race, and age. For white women, the crude prevalence rate of unexplained chronic fatigue ranged from 28.6 cases per 100,000 population in Atlanta to 60.0 per 100,000 in Wichita, with an overall prevalence of 37.3 per 100,000. The overall crude prevalence rate of chronic fatigue for white men was 7.0 cases per 100,000. The rank orders of prevalence of CFS and unexplained chronic fatigue for the four surveillance sites were the same using both crude and the adjusted rates.

Incidence

An incident case was defined as a case of CFS in a patient (i.e., illness in a patient assigned to Group I) who had onset of symptoms during the 4-year surveillance period. Only 19 incident cases were identified: 10 in Atlanta, four in Wichita, four in Grand Rapids, and one in Reno. The overall annual incidence rates, as well as the site-specific annual incidence rates, were less than one case per 100,000 persons. The rates of CFS for the four surveillance sites were not significantly different, and the rates remained stable during the 4-year surveillance period.

TABLE 3. Percentage of patients* participating in the chronic fatigue syndrome (CFS) surveillance system who reported CFS symptoms and signs, by diagnostic category[†] — four U.S. cities,[§] September 1989 through August 1993

	Diagnostic category				
Symptoms/Signs	Group I	Group II	Group III	Group IV	Total
Symptoms					
Neurocognitive complaints	98	87	96	92	95
Fever and/or chills	96	61	80	76	80
Sore throat	92	41	68	71	69
Myalgia	88	58	80	75	78
Sleep disturbance	92	61	84	83	81
Muscle weakness	88	55	75	70	74
Swollen lymph nodes	84	33	62	65	62
Unusual fatigue	81	37	64	67	64
Arthralgia	81	37	66	62	64
Headache	73	35	60	60	59
Sudden onset	37	22	29	44	32
Signs					
Palpable lymph nodes	32	17	16	17	20
Nonexudative pharyngitis	24	15	12	15	6
Fever	5	2	4	4	4

*Persons aged ≥18 years.
[†]Patients were assigned to one of four groups: those whose illnesses met the criteria of the 1988 CFS case definition (Group I); those whose fatigue or symptoms did not meet the criteria for CFS (Group II); those who had had an identifiable psychological disorder before onset of fatigue (Group III); and those who had evidence of a medical condition that could have caused fatigue (Group IV).
[§]Atlanta, Georgia; Wichita, Kansas; Grand Rapids, Michigan; and Reno, Nevada.

DISCUSSION

This surveillance system demonstrated the feasibility of conducting surveillance for an illness characterized primarily on the basis of self-reported symptoms. This system identified the existing CFS cases in those patients who were referred to the system at the four surveillance sites. The annual number of CFS incident cases did not increase during the surveillance period.

The mean age of the CFS patients at the time of symptom onset, 30 years, was similar to that reported previously (9,12). The 6.7-year average duration of fatiguing illness before participation in this surveillance system was consistent with the reported long-term nature of CFS (15). Less than 8% of the CFS patients reported an eventual absence of all symptoms during the surveillance period. If recovery from CFS is reflected by the absence of symptoms, then the 4-year period prevalence estimates should provide an estimate of point prevalence for August 31, 1993 (i.e., the last day of the surveillance period).

The results of several previously published studies indicated that CFS occurs primarily among white females (12,15,16), and the high percentage of CFS patients who were white women in the CDC surveillance system for CFS was consistent with these

TABLE 4. Prevalence rates* of chronic fatigue syndrome — four U.S. cities, September 1989 through August 1993

City	All cases		Cases in white women	
	Crude	Adjusted[†]	Crude	Adjusted[§]
Atlanta, GA	3.8	4.0	8.6	8.8
Grand Rapids, MI	6.1	6.3	10.7	11.9
Reno, NV	7.4	6.7	14.1	15.3
Wichita, KS	9.6	8.7	17.7	19.5
Total	**5.2**	**6.4**	**10.8**	**13.9**

*Prevalence rates for the 4-year period per 100,000 persons aged ≥18 years.
[†]Adjusted for age, race, and sex.
[§]Adjusted for age.

TABLE 5. Prevalence rates* of chronic fatiguing illness[†] — four U.S. cities, September 1989 through August 1993

City	All cases		Cases in white women	
	Crude	Adjusted[§]	Crude	Adjusted[¶]
Atlanta, GA	12.9	13.7	28.6	29.1
Grand Rapids, MI	19.5	18.6	36.1	39.7
Reno, NV	32.6	29.1	57.3	60.3
Wichita, KS	34.3	31.4	60.1	65.7
Total	**18.4**	**23.2**	**37.3**	**48.7**

*Prevalence rates for the 4-year period per 100,000 persons aged ≥18 years.
[†]Includes persons who have chronic fatigue syndrome.
[§]Adjusted for age, race, and sex.
[¶]Adjusted for age.

reports. Previous reports also indicated that persons who have CFS are more likely to be well-educated and are potentially high-income earners (*12,15,16*). Of the CFS patients identified by the surveillance system, 96% had graduated from high school, and 38% of this group had graduated from college. Although 48% of CFS patients were unemployed at the time of interview, the median annual household income of these patients was $40,000. However, the higher prevalence of CFS among some groups in this study (e.g., white women) could reflect selection biases. For example, the education and income levels of the patients participating in the surveillance system could have influenced their pattern of using the health-care system (i.e., persons with lower incomes who had a fatiguing illness might not have sought medical care for the illness and would not have been referred to the surveillance system).

The number and pattern of symptoms reported by patients in Groups I, III, and IV were similar, suggesting that the criteria of the CFS case definition do not enable clinicians to reliably distinguish which patients have a history of a psychological disorder. The National Institutes of Health (*17*) and CDC (*18*) have recommended that future studies of fatiguing illness continue to include patients both with and without a history of a psychological disorder so that information regarding these groups can be analyzed separately.

The physical signs listed in the CFS case definition were not useful for classifying CFS cases. Only seven (5%) of the CFS cases were classified as such based on the presence of physical signs. Furthermore, no specific symptom or group of symptoms enabled CFS to be distinguished from illness in patients assigned to the other groups. Illnesses in Group I patients might represent one end of a CFS spectrum (i.e., the most severe degree of illness), whereas illnesses in Group II patients might represent the other end (i.e., the least severe). By definition, the Group II patients reported fewer CFS symptoms, but this group also reported substantially fewer symptoms not included in the CFS case definition.

The crude estimates of the 4-year period prevalence of CFS ranged from 3.8 to 9.6 cases per 100,000 population. These estimates could not be compared with the prevalence of 7.4 per 100,000 reported previously (*10*) because this latter estimate a) was based on an approximation to the CDC CFS case definition and b) represented a lifetime prevalence. Because of the long duration of CFS, the period prevalence estimates derived from the CDC surveillance system can be more appropriately compared with the point prevalence estimates derived from the study conducted in Australia (*9*). Although the overall period prevalence estimate of CFS in the four U.S. cities (i.e., 5.2 cases per 100,000 population) was lower than the point prevalence estimate reported for the study in Australia (37.1 per 100,000), the CFS case definition used in the CDC surveillance system was more restrictive. The CDC classification for unexplained chronic fatigue more closely approximated the CFS case definition used in the study conducted in Australia (*19*), and the site-specific period prevalence estimates of unexplained chronic fatigue in the four U.S. cities (i.e., 11.3–27.8 cases per 100,000 population) were comparable to the point prevalence estimate of CFS derived from the study conducted in Australia (*9*).

Reno was chosen as a surveillance site because of its close proximity to Incline Village (i.e., the site of the first CDC investigation of a cluster of CFS cases) and because of concern regarding the incidence of CFS in this geographic area (*4*). The

prevalence of CFS in Reno, however, was similar to the prevalence in the other surveillance sites, and the incidence of CFS in this area was the lowest among the sites.

This CFS surveillance system demonstrated the feasibility of collecting information concerning the demographic characteristics of participants and estimating a 4-year period prevalence for both CFS and unexplained prolonged fatigue. However, the possible underascertainment of CFS cases in this study may have biased these estimates downward; all the estimated rates should, therefore, be considered minimum estimates of the true prevalence of CFS and unexplained chronic fatigue in the four U.S. cities.

At least six factors could have been associated with underreporting of CFS cases. First, some physicians who treat patients who have CFS might not have been asked to participate in the surveillance system. However, current telephone and medical directories were used to identify such physicians, and all these physicians were contacted and asked to participate in the surveillance system. In addition, physicians who were identified during the surveillance period were asked to participate, and contact was maintained with participating physicians during the surveillance period to encourage continued participation. Second, approximately 50% of all physicians who were asked to participate chose not to do so; however, most of these physicians reported that they either a) did not provide service to patients who have CFS or b) did not accept CFS as an established diagnosis. Third, follow-up surveys of the 489 participating physicians indicated that, of the 241 physicians who provided service to patients who should have been referred to the surveillance system, 22 (9%) physicians did not refer such patients. Fourth, participating physicians might have referred only those patients whose illness was probably CFS, rather than all patients whose illness met the screening criteria (i.e., >67% of patients reported that their illness had been diagnosed as CFS by the physician before the referral). Fifth, 13% of the patients who had been referred to the surveillance system chose not to participate. Finally, many patients who had a fatiguing illness might not have sought medical care; however, a CDC survey conducted in 1994 indicated that 82% of persons who had unexplained chronic fatigue sought medical care for the illness (CDC, unpublished data). All these factors could have contributed to an underestimation of the prevalence of CFS and unexplained chronic fatigue in the four surveillance sites. However, these prevalence estimates, even if understated, are similar to previously reported estimates (9).

The sites chosen for this surveillance system were not selected randomly; therefore, the findings cannot be directly generalized to the overall U.S. population. The range of prevalence estimates for the four sites might reflect actual differences between the sites or differences in case ascertainment. An additional limitation of this surveillance system was the potential for inaccurate recall of information by patients, whose average illness duration at the time of interview was >6 years. However, many patients kept extensive records of their fatiguing illness and were able to provide detailed information regarding the onset of symptoms. Future studies of CFS should include patients who have more recent onset of illness to minimize the potential for recall bias.

Despite the limitations, this surveillance system will assist in investigations of CFS and its impact on patients who have the illness. In February 1997, CDC began a large-scale, cross-sectional study at one surveillance site (Wichita) to describe more completely the magnitude and epidemiology of CFS. The population-based approach

will enable investigators to actively and more completely identify patients who have CFS and unexplained chronic fatigue. Information concerning these patients can then be compared with information for persons in the same population who do not have chronic fatigue.

Acknowledgments

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Tetanus Surveillance — United States, 1991–1994

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Abstract

Problem/Condition: Despite the widespread availability of a safe and effective vaccine against tetanus, 201 cases of the disease were reported during 1991–1994. Of patients with known illness outcome, the case-fatality rate was 25%.

Reporting Period Covered: 1991–1994.

Description of System: Physician-diagnosed cases of tetanus are reported to local and state health departments, the latter of which reports these cases on a weekly basis to CDC's National Notifiable Disease Surveillance System. Since 1965, state health departments also have submitted supplemental clinical and epidemiologic information to CDC's National Immunization Program.

Results: During 1991–1994, 201 cases of tetanus were reported from 40 states, for an average annual incidence of 0.02 cases per 100,000 population. Of the 188 patients for whom age was known, 101 (54%) were aged ≥60 years and 10 (5%) were aged <20 years. No cases of neonatal tetanus were reported. Among adults, the risk for tetanus increased with age; the risk for persons aged ≥80 years was more than 10 times greater than the risk for persons aged 20–29 years. All deaths occurred among persons aged ≥30 years. The case-fatality rate (overall: 25%) increased with age, from 11% in persons aged 30–49 years to 54% in persons aged ≥80 years. Only 12% of all patients were reported to have received a primary series of tetanus toxoid before onset of illness. For 77% of patients, tetanus occurred after an acute injury was sustained. Of patients who obtained medical care for their injury, only 43% received tetanus toxoid as part of wound prophylaxis.

Interpretation: The epidemiology of reported tetanus in the United States during 1991–1994 was similar to that during the 1980s. Tetanus continued to be a severe disease primarily of older adults who were unvaccinated or inadequately vaccinated. Most tetanus cases occurred after an acute injury was sustained, emphasizing the need for appropriate wound management.

Actions Taken: In addition to decennial booster doses of tetanus-diphtheria toxoid during adult life, the Advisory Committee on Immunization Practices (ACIP) recommends vaccination visits for adolescents at age 11–12 years and for adults at age

50 years to enable health-care providers to review vaccination histories and administer any needed vaccine. Full implementation of the ACIP recommendations should virtually eliminate the remaining tetanus burden in the United States.

INTRODUCTION

The reported incidence of tetanus has declined substantially since the mid-1940s, when tetanus toxoid (TT) became available for widespread use (*1,2*). This decline in tetanus incidence followed a) the widespread use of both tetanus toxoid (TT)-containing vaccines formulated as diphtheria and tetanus toxoids and whole-cell pertussis vaccine (DTP) and diphtheria and tetanus toxoids (DT) for infants and children and diphtheria and tetanus toxoid (Td) for adults, b) the use of TT and tetanus immune globulin (TIG) for postexposure prophylaxis in wound treatment, and c) improved wound care and management. Furthermore, the proportion of the U.S. population residing in urban areas has increased during the 1900s (*3*), resulting in decreased exposure to tetanus spores; this decreased exposure possibly contributed to the decline in tetanus mortality.

Major efforts have been made to increase immunization coverage among children in the United States. All 50 states have passed legislation requiring that children be vaccinated for tetanus before admission to school (*4*), and >96% of school-aged children have received three or more DTP vaccinations by the time they begin school (*1*). Vaccination rates historically have been lower for preschool children aged <5 years (*1,4*). Since 1991, initiatives to improve immunization coverage among preschool children have substantially increased immunization levels among 2-year-old children (*5*). In 1994, 93% of children aged 19–35 months had been vaccinated with three doses of either DTP or pediatric DT (*6*). Vaccination coverage among elderly persons remains low (*7*).

CDC conducts surveillance for tetanus to monitor the epidemiology of the disease and to identify persons at greatest risk. This report describes an analysis of reported tetanus cases in the United States for 1991–1994 and evaluates long-term trends of disease incidence since 1947.

METHODS

Tetanus Surveillance

Tetanus surveillance relies on the passive reporting of physician-diagnosed cases to local and state health departments. Because a laboratory assay to enable a definitive diagnosis of tetanus is not routinely available, the diagnosis is based on the clinical judgment of the attending physician. Before 1990, the clinical case definition of tetanus was "physician-diagnosed tetanus." In 1990, this definition was revised, for the purposes of public health surveillance, to include illness characterized by an acute onset of hypertonia and/or painful muscular contractions (usually of the muscles of the jaw and neck) and generalized muscle spasms without other apparent medical cause (*8*).

State health departments report cases of tetanus on a weekly basis to CDC's National Notifiable Disease Surveillance System (NNDSS). CDC publishes the number of cases reported by each state to the NNDSS on a weekly basis and in an annual summary (*2*). In addition, state health departments report supplemental clinical and epidemiologic information for each case to CDC's National Immunization Program (NIP). This supplemental reporting system, which was initiated in 1965, provides CDC with information concerning the clinical history, presence and nature of any associated risk factors, vaccination status of the patient, wound care, and clinical management for each tetanus case (*9*). A summary of this additional information is published every 2–3 years (*10–13*).

Data Analysis

The differences between medians were tested by using the Wilcoxon rank sum test statistic (*14*). A p-value of <0.05 was considered statistically significant.

RESULTS

Long-Term Trends

The national tetanus surveillance system documented a decrease in tetanus morbidity from 560 reported cases in 1947 (i.e., the year national reporting of tetanus cases was initiated) to fewer than 50 cases in both 1992 and 1993 (Figure 1). However, since 1976, the rate of decline of reported tetanus incidence has been slower. The incidence rate for 1991–1994 was similar to that for 1987–1990. The overall case-fatality rate also has declined, from 91% in 1947 to 44% in 1976 and to 24% in 1989–1990. Since 1990, the overall case-fatality rate has remained relatively unchanged (i.e., 25% overall for 1991–1994).

Epidemiology

During 1991–1994, 201 tetanus cases were reported to the NNDSS (i.e., 57 cases in 1991, 45 in 1992, 48 in 1993, and 51 in 1994). The average annual incidence rate for 1991–1994 was 0.02 cases per 100,000 population; this rate represents a 95% decrease from the 0.39 cases per 100,000 population reported for 1947.

At least one case of tetanus was reported by each of 39 states and the District of Columbia during 1991–1994 (Figure 2), and tetanus cases were reported all 4 years by eight states (California, Florida, Illinois, Michigan, Minnesota, Ohio, Pennsylvania, and Texas). No cases were reported in 11 states; six (55%) of these states are located in the Rocky Mountain and West North Central regions (i.e., regions in which the reported incidence of tetanus was low in previous years [*10–13*]).

Supplemental information was provided for 192 (96%) of the 201 reported tetanus cases. Of the 189 patients for whom sex was reported, 99 (52%) were female. Of 188 patients for whom age was reported, 101 (54%) were aged ≥60 years, and 10 (5%) were aged <20 years (Figure 3). Six cases occurred in children aged <15 years. No cases of neonatal tetanus were reported. The youngest patient was an unvaccinated 6-year-old boy who had sustained a puncture wound in his foot. He had generalized

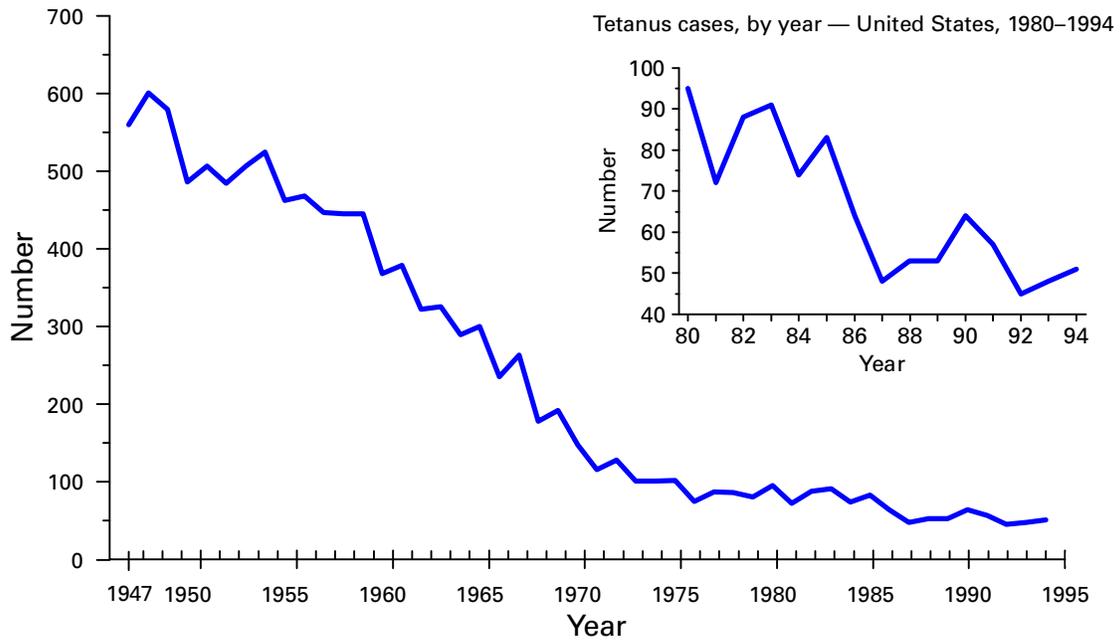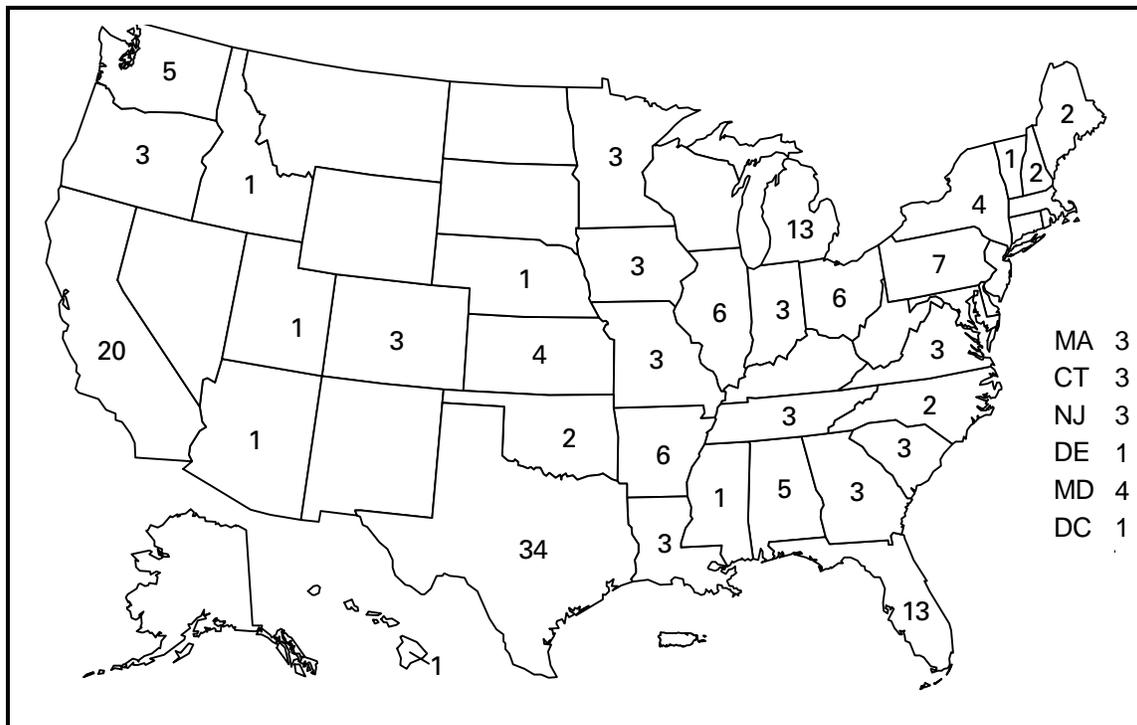**FIGURE 1. Reported number of tetanus cases, by year — United States, 1947–1994**

Tetanus cases, by year — United States, 1980–1994

FIGURE 2. Reported number of tetanus cases, by state — United States,* 1991–1994

MA	3
CT	3
NJ	3
DE	1
MD	4
DC	1

*Cases were reported from 39 states and the District of Columbia.

tetanus that required mechanical ventilation; he recovered after a 1-month hospitalization.

A total of 46 deaths occurred among the 185 patients whose illness outcome was known (case-fatality rate: 25%). All tetanus-related deaths occurred among persons aged ≥30 years. The case-fatality rate increased with age, from 11% in persons aged 30–49 years to 54% in persons aged ≥80 years.

Type of Tetanus

The type of tetanus was reported for 150 cases. Of these cases, 121 (81%) were generalized, 20 (13%) were localized, and nine (6%) were cephalic tetanus.

Previous Vaccination Status

Tetanus vaccination status was known for 89 (46%) of the 192 patients, and age was known for 86 (97%) of these 89 patients. Of the nine patients aged <20 years for whom vaccination status was reported, five had received no previous doses of a TT-containing vaccine, three had received four doses, and one had received five doses. Of the 77 patients aged ≥20 years for whom this information was reported, 42 (55%) had received no previous doses of TT, 17 (22%) had received a single dose, and 18 (23%) had received at least three doses.

FIGURE 3. Reported number of tetanus cases, average annual incidence rates,* and survival status of patients, by age group — United States, 1991–1994
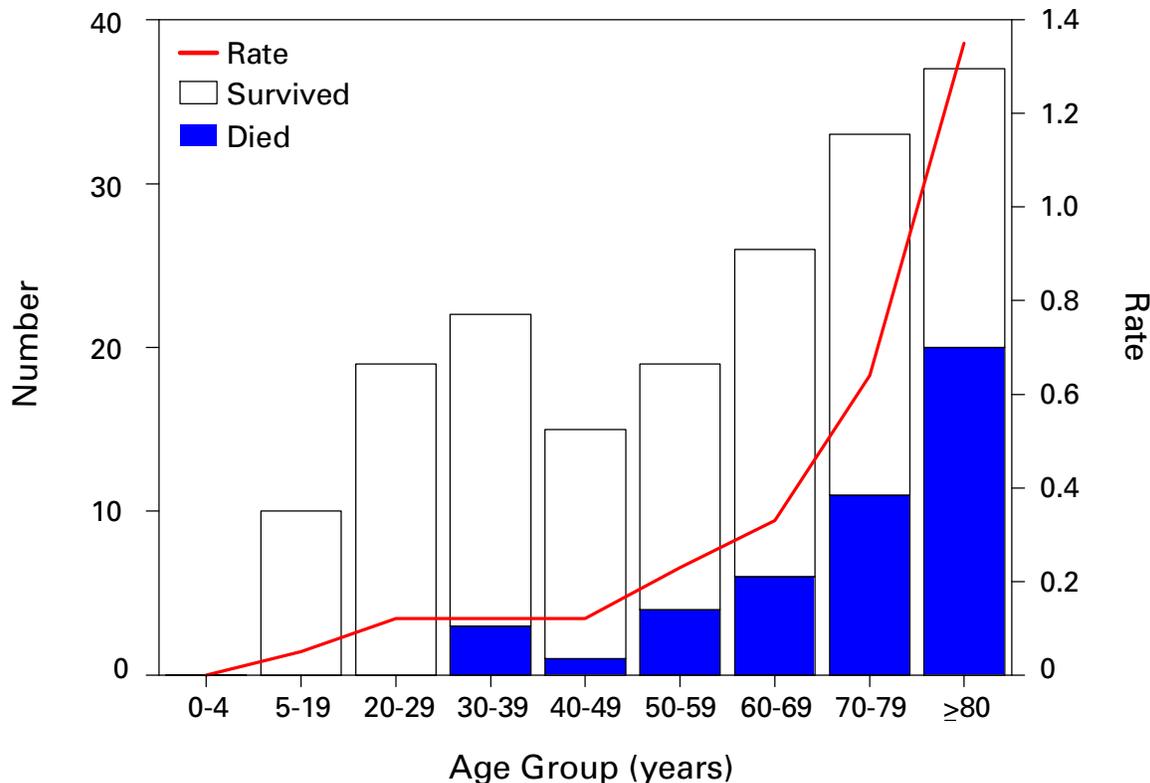
*Per 100,000 population.

Twenty-three (12%) of the 192 patients were reported to have received at least a primary series (i.e., three or more doses) of TT before onset of illness (Table 1). Of these patients, 13 were reported to have received the last booster ≤10 years before onset of illness. For two patients, this information was verified by records obtained from their primary health-care providers. The first patient was a 12-year-old girl who had onset of illness during 1994. She had previously received five doses of DTP, the last of which was received 4 years before onset of illness. She was not hospitalized, and she recovered without sequelae after 6 weeks of home care. The second patient was a 29-year-old man who had a history of amphetamine abuse. He had previously received four doses of a TT-containing vaccine, the last dose of which was received 6 years before onset of illness. He also recovered.

Two cases occurred in persons who did not receive vaccination because of religious objections (i.e., a 12-year-old boy in Montgomery, Georgia, and a 17-year-old boy in Lancaster, Pennsylvania). Both patients had generalized forms of tetanus and required mechanical ventilation.

Type of Injury, Wound Treatment, and Prophylaxis

An acute injury sustained before onset of illness was identified for 148 (77%) of the 192 tetanus cases. Of these cases, 72 (49%) occurred after puncture wounds. The most frequently reported type of puncture wound was sustained by stepping on a nail, which was reported by 23 (16%) of all patients who had sustained an identified acute injury. The other most frequently reported types of acute injury were lacerations (20%) and abrasions (12%). Five patients had been bitten or scratched by animals, including one patient who reported having been scratched in the face by a peacock.

The site of the antecedent acute injury was a lower extremity in 77 (52%) cases, an upper extremity in 50 (34%) cases, and the head or trunk in eight (5%) cases. The injury site was not specified for 13 cases.

The median incubation period was 7 days (range: 0–90 days) for the 138 patients for whom the dates of both the antecedent injury and the onset of illness were specified. The incubation period was ≤45 days for all but one case, which occurred in a 64-year-old woman who was on long-term immunosuppressive therapy and whose immunization status was unknown. This woman had been bitten on one of her legs by a dog 90 days before onset of illness, and her wound ulcerated. She died after 75 days of treatment. The incubation period for most (101 [73%]) of the 138 tetanus cases ranged from 4 to 14 days; this period was ≤3 days for 21 (15%) cases and >14 days for 16 (12%) cases.

TABLE 1. Tetanus toxoid vaccination status of persons with reported tetanus — United States, 1991–1994

Vaccination status	No.	(%)
0 doses	49	(25.5)
1 dose	17	(8.9)
2 doses	0	(0.0)
3 doses	5	(2.6)
≥4 doses	18	(9.4)
Unknown	103	(53.6)
Total	**192**	**(100.0)**

The environment in which the antecedent injury occurred was reported for 117 patients. Of these patients, 57 (49%) were injured while indoors; 36 (31%), while performing outdoor farming or gardening activities; and 23 (20%), while engaged in other outdoor activities. One (1%) patient had sustained motor-vehicle–related injuries.

Information regarding medical care was reported for 135 patients who became ill with tetanus after sustaining an acute wound; of these patients, 51 (38%) had obtained medical care for the injury. TT was administered as prophylaxis to 22 patients (i.e., 43% of those who obtained medical care), 15 (68%) of whom received toxoid within 4 days after the injury. In accordance with the recommendations of the Advisory Committee on Immunization Practices (ACIP) for the use of adult formulation Td and TIG in wound management (Table 2) (32), 22 (92%) of the 24 patients who had obtained medical care for an acute injury but were not administered Td should have received the toxoid. Information regarding administration of toxoid was unavailable for the remaining five patients.

Thirteen patients who had acute wounds severe enough to have received prophylactic wound debridement were candidates for both Td and TIG (Table 2); five of these patients were administered Td in the course of wound management, and three were administered TIG.

Twenty-three cases unrelated to acute injury were associated with either diabetes (seven patients, five of whom were insulin-dependent) or chronic wounds (e.g., skin ulcers, abscesses, or gangrene) (21 patients). Five patients were reported as having both diabetes and a chronic wound. The only risk factor associated with tetanus for one patient was a history of parenteral drug abuse.

Surgery performed 3–21 days before onset of illness was reported for seven patients; for six of these patients, it was the only reported risk factor for tetanus (the other patient had concomitant insulin-dependent diabetes mellitus). For these cases, the median interval between surgery and onset of illness was 7 days (range: 2–13 days). None of these patients were known to have received TT during the 10 years preceding the surgery. One patient had surgery performed on the leg; three

TABLE 2. Summarized recommendations for the use of tetanus prophylaxis in routine wound management — Advisory Committee on Immunization Practices (ACIP), 1991 (7)

History of adsorbed tetanus toxoid	Clean, minor wounds		All other wounds*	
	Td[†]	TIG[§]	Td	TIG
Unknown or <3 doses	Yes	No	Yes	Yes
≥3 doses[¶]	No**	No	No[††]	No

*Such as, but not limited to, wounds contaminated with dirt, feces, soil, or saliva; puncture wounds; avulsions; and wounds resulting from missiles, crushing, burns, or frostbite.

[†]For children aged <7 years; the diphtheria and tetanus toxoids and pertussis vaccine (DTP)—or pediatric diphtheria and tetanus toxoids (DT), if pertussis vaccine is contraindicated—is preferred to tetanus toxoid (TT) alone. For persons aged ≥7 years, the tetanus and diphtheria toxoids (Td) for adults is preferred to TT alone.

[§]TIG=tetanus immune globulin.

[¶]If only three doses of *fluid* toxoid have been received, a fourth dose of toxoid—preferably an adsorbed toxoid—should be administered.

**Yes, if >10 years have elapsed since last dose.

[††]Yes, if >5 years have elapsed since last dose. (More frequent boosters are not needed and can accentuate side effects.)

patients, the hips and sacral area; and three patients, the abdomen (i.e., by laparotomy). The mean age of patients who had undergone surgery was 51 years (range: 21–77 years). One patient, an unimmunized 63-year-old woman who had had toe surgery, died as a result of tetanus. Information regarding acute injury, chronic wound, or other preexisting medical conditions was unavailable for 14 patients.

Clinical Features and Treatment

Information concerning therapeutic use of TIG was available for 168 patients; of these patients, 163 (97%) reported having received TIG. The exact dosage of TIG was specified for 115 (71%) of the 163 patients; the median dosage used therapeutically was 3,000 IU (range: 250–10,000 IU). The time interval between onset of illness and TIG administration was known for 146 of the patients who received TIG; TIG was administered to 42 (29%) of these patients <24 hours after onset of illness and to 52 (36%) patients from 1 to 4 days after onset. Information concerning illness outcome was reported for 157 patients who received TIG; 35 (22%) of these patients died. Two (40%) of the five patients who did not receive TIG died. This difference was not statistically significant (relative risk [RR]=0.56; 95% confidence interval [CI]=0.18<RR<1.7). Initial (Wilcoxon rank sum test: p=0.67) or total (Wilcoxon rank sum test: p=0.46) dosage of TIG did not differ significantly between patients who died and those who recovered.

The length of hospitalization was reported for 131 patients; the median duration was 15 days (range: 0–92 days). Information regarding the use of assisted ventilation was available for 151 patients; of these patients, 101 (67%) required ventilation. Information concerning both the outcome and the use of assisted ventilation was available for 145 patients; of these, 29 (30%) of the 98 patients who required ventilation died, compared with two (4%) of the 47 who did not require ventilation.

The direct costs of medical care were assessed for the 10 cases reported by Texas during 1991; the median cost was $65,651 (range: $12,099–$154,200) (J. Pelosi, Texas Department of Health, personal communication). The cost of hospitalization, including physicians' fees, for the two tetanus cases reported by Kansas during 1993 was $145,329 and $151,492 (*15*).

DISCUSSION

The epidemiology of reported tetanus in the United States during 1991–1994 was similar to that during the 1980s (*10–13*). Tetanus continued to be a severe disease primarily of older adults who were unvaccinated or inadequately vaccinated. Data obtained from a national population-based serologic survey (*16*) indicate that the prevalence of immunity to tetanus in the United States is lower in older age groups, from >80% among persons aged 6–39 years to 28% among persons aged ≥70 years. Previous serologic studies also have indicated that older adults lack protective levels of tetanus antibodies (*17–19*) and that elderly persons who reside in rural areas are more likely to be unimmunized than elderly persons in urban areas (*20*).

Tetanus is preventable through both vaccination and appropriate wound prophylaxis. Vaccination with a primary series of three doses of TT-containing vaccine and booster doses of Td every 10 years is highly effective in preventing tetanus (*21*).

During 1991–1994, only 26% of patients with known vaccination history had completed a primary series of TT before onset of tetanus, and in only two cases was vaccination against tetanus in the 10 years preceding onset of tetanus verified.

Tetanus remains a clinical diagnosis because confirmatory laboratory tests are not available for routine use. Isolation of the organism from wounds is neither sensitive nor specific, because a) anaerobic cultures of tissues or aspirates usually are not positive and b) the organism might be grown from wounds in the absence of clinical signs and symptoms of disease (*22–24*).

The number of tetanus cases derived from passive reporting by physicians to local and state health departments underestimates the true incidence of tetanus in the United States. Completeness of reporting for tetanus mortality has been estimated at 40%, while completeness of reporting for tetanus morbidity may be even lower (*25*). Although tetanus reporting is incomplete, an analysis of tetanus mortality reporting suggests that the reported tetanus cases are representative of all tetanus cases (*25*).

As noted previously (*10–13*), most (77%) tetanus cases occurred after an acute injury was sustained; stepping on a nail was the most frequent cause of these injuries. Acute-wound–associated tetanus can be prevented by appropriate wound management, including active and/or passive immunization. Only 38% of patients for whom this information was available had obtained medical care for the acute injury; according to current ACIP recommendations (Table 2), 43% of these patients should have received prophylaxis but did not. Approximately half the antecedent injuries occurred indoors, emphasizing the need to consider such injuries as being risk factors for tetanus. The median incubation period between the antecedent injury and onset of tetanus was 7 days; in all but one case, this time period was <45 days. More than 80% of cases were diagnosed as generalized tetanus.

No cases of neonatal tetanus were reported during this 4-year period. Only one case of neonatal tetanus, which occurred during 1989 in an infant born to an unvaccinated mother, was reported during 1984–1994 (*10–13*). Although almost all tetanus cases in the United States occur in adults, most reported cases of tetanus worldwide occur as neonatal tetanus (*26–28*). Neonatal tetanus can be prevented through maternal vaccination and hygienic delivery practices, and the World Health Organization has targeted neonatal tetanus for elimination (*27,28*).

When immunization programs are in place, the age distribution of patients usually reflects the remaining susceptibility to the infection in the population (*29*). During 1991–1994, two tetanus cases occurred in persons aged 12 and 17 years who were members of communities that object to vaccination. Persons who object to vaccination because of religious or philosophical beliefs may disproportionately contribute to the remaining tetanus burden in the United States (*30*).

During 1991–1994, more than half the total number of reported cases occurred in persons aged ≥60 years. In January 1994, the National Vaccine Advisory Committee concluded that vaccine-preventable diseases among adults in the United States were a continuing cause of morbidity and mortality, particularly among older persons (*31*). Adult immunization levels may be markedly increased by reducing missed opportunities to vaccinate adults during health-care visits (*32*). During 1991–1994, recent surgery was the only known injury for seven (4%) patients; TT had not been administered preoperatively to these patients, although none had a history of vaccination during the preceding 10 years. Because persons of all ages are exposed to tetanus,

maintaining protection against tetanus (and diphtheria) after the primary series can be achieved by routinely scheduling booster doses of Td at decade ages (e.g., at 30, 40, and 50 years of age) (*7*).

ACIP recommended recently that persons be routinely scheduled for a vaccination visit at age 11–12 years and age 50 years (*33*). Such visits enable health-care providers to a) review the patient's vaccination status, b) administer Td as indicated, and c) determine whether a patient needs other vaccinations, such as influenza and pneumococcal vaccinations (*34,35*). Full implementation of these recommendations and compliance with the decennial Td booster policy should virtually eliminate the remaining tetanus burden in the United States.

Acknowledgments

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Malaria Surveillance — United States, 1993

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Abstract

Problem/Condition: Malaria is caused by infection with one of four species of *Plasmodium* (*P. falciparum, P. vivax, P. ovale,* and *P. malariae*), which are transmitted by the bite of an infective female *Anopheles* sp. mosquito. Most malaria cases in the United States occur among persons who have traveled to areas (i.e., other countries) in which disease transmission is ongoing. However, cases are transmitted occasionally 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.

Reporting Period Covered: Cases with onset of illness during 1993.

Description of System: Malaria cases confirmed by blood smear are reported to local and/or state health departments by health-care providers and/or laboratories. Case investigations are conducted by local and/or state health departments, and the reports are transmitted to CDC.

Results: CDC received reports of 1,275 cases of malaria in persons in the United States and its territories who had onset of symptoms during 1993; this number represented a 40% increase over the 910 malaria cases reported for 1992. *P. vivax, P. falciparum, P. ovale,* and *P. malariae* were identified in 52%, 36%, 4%, and 3% of cases, respectively. The species was not determined in the remaining 5% of cases. The 278 malaria cases in U.S. military personnel represented the largest number of such cases since 1972; 234 of these cases were diagnosed in persons returning from deployment in Somalia during Operation Restore Hope. In New York City, the number of reported cases increased from one in 1992 to 130 in 1993. The number of malaria cases acquired in Africa by U.S. civilians increased by 45% from 1992; of these, 34% had been acquired in Nigeria. The 45% increase primarily reflected cases reported by New York City. Of U.S. civilians who acquired malaria during travel, 75% had not used a chemoprophylactic regimen recommended by CDC for the area in which they had traveled. Eleven cases of malaria had been acquired in the United States: of these cases, five were congenital; three were induced; and three were cryptic, including two cases that were probably locally acquired mosquito-borne infections. Eight deaths were associated with malarial infection.

Interpretation: The increase in the reported number of malaria cases was attributed to a) the number of infections acquired during military deployment in Somalia and b) complete reporting for the first time of cases from New York City.

Actions Taken: Investigations were conducted to collect detailed information concerning the eight fatal cases and the 11 cases acquired in the United States. Malaria prevention guidelines were updated and disseminated to health-care providers. Persons who have a fever or influenza-like illness after returning from a malarious area should seek medical care, regardless of whether they took antimalarial chemoprophylaxis during their stay. The medical evaluation should include a blood smear examination for malaria. Malaria can be fatal if not diagnosed and treated rapidly. Recommendations concerning prevention and treatment of malaria can be obtained from CDC.

INTRODUCTION

Malaria is caused by infection with one of four species of *Plasmodium* (*P. vivax, P. falciparum, P. ovale,* and *P. malariae*). Infection is transmitted by the bite of an infective female *Anopheles* sp. mosquito. Forty percent of the world's population live in areas where malaria is transmitted (e.g., parts of Africa, Asia, Central America, Hispaniola, North America, Oceania, and South America). In the past, malaria was endemic throughout much of the continental United States. During the late 1940s, a combination of improving socioeconomic conditions, water management, vector-control efforts, and case management was successful at interrupting malaria transmission in the United States (*1*). Since then, malaria case surveillance has been maintained to detect locally acquired cases that could indicate reintroduction of mosquito-borne transmission.

Through 1993, almost all cases of malaria diagnosed in the United States were imported from regions of the world where malaria transmission was known to occur. Each year, a few congenital infections and infections resulting from exposure to infected blood and blood products have been acquired in the United States. In addition, outbreaks of malaria that were probably acquired through local mosquito-borne transmission were identified during 1989–1992 (i.e., California, outbreaks in 1988, 1989, and 1990; Florida, 1990; and New Jersey, 1991) (*2–4*).

State and/or local health departments and CDC thoroughly investigate all malaria cases acquired in the United States, and CDC conducts an analysis of all imported malaria cases to detect trends in acquisition. This information has been used to guide recommendations for preventing malaria among persons who travel abroad. For example, an increase in *P. falciparum* malaria among travelers returning from Africa, an area with increasing incidence of chloroquine-resistance, prompted CDC in 1990 to change the recommended chemoprophylaxis from chloroquine to mefloquine (*5*). This report summarizes malaria cases reported to CDC for 1993.

METHODS

Sources of Data

Malaria surveillance is a passive system; cases of blood-slide–confirmed malaria are identified by health-care providers, infection-control practitioners, and/or laboratories. A slide-confirmed case is reported to local and/or state health departments, and a standard form that contains clinical, laboratory, and epidemiologic information is completed. This information is transmitted to the state health department and then to CDC. CDC staff review all report forms at the time of receipt and request additional information if necessary (e.g., if no recent travel is reported or chemoprophylaxis failure is suspected). CDC directly obtains reports of other cases from health-care providers who request assistance with the diagnosis and treatment of malaria. In addition, records of CDC's National Malaria Reference Laboratory are reviewed, and case report forms are completed for all patients who have smear-positive infection that have not already been reported. All cases that have been acquired in the United States are fully investigated, including all induced and congenital cases and possible introduced or cryptic cases. Information derived from uniform case report forms concerning all slide-confirmed cases is entered into a computer data base and analyzed annually.

Definition of Terms

The following definitions are used in this report:

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

- **Confirmed case:** Symptomatic or asymptomatic illness that occurs in the United States in a person who has microscopically 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.*

This report also uses terminology derived from the recommendations of the World Health Organization (WHO) (*6*). Definitions of the following terms are included for reference.

- **Autochthonous malaria:**

  - **Indigenous.** Malaria acquired by mosquito transmission in an area where malaria occurs regularly.

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*To confirm the diagnosis of blood smears 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 Section; telephone (770) 488-7760.

— **Introduced.** Malaria acquired by mosquito transmission 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.

- **Induced malaria:** Malaria acquired through artificial means (e.g., blood transfusion, common syringes, or malariotherapy).

- **Relapsing malaria:** Renewed manifestation (i.e., of clinical symptoms and/or parasitemia) of malarial infection that is separated from previous manifestations of the same infection by an interval greater than those caused by 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 diagnosis of malaria requires that physicians consider malaria in the differential diagnosis of every patient who has an unexplained fever; the evaluation of such patients should include taking a comprehensive travel history. If malaria is suspected, a Giemsa-stained smear of the patient's peripheral blood should be examined for parasites. Thick and thin blood smears must be prepared properly because the accuracy of diagnosis depends on the quality of the blood film and the experience of the laboratory personnel. (See Appendix for proper procedures necessary for accurately diagnosing malaria.)

RESULTS

General Surveillance

CDC received reports of 1,275 malaria cases that had onset of symptoms during 1993 among persons in the United States and its territories. This represented a 40% increase over the 910 cases of malaria reported for 1992 and was the highest total number of cases reported to CDC since 1980 (7). In 1993, 11 of the 1,275 cases had been acquired in the United States.

Since 1973, malaria in civilians has accounted for most cases reported to CDC (Table 1). During 1993, 519 (41%) reported cases of malaria were diagnosed in U.S. civilians, representing a 31% increase from the 394 cases reported for 1992 (Figure 1). The 453 (36%) malaria cases in foreign civilians constitutes a 6% decrease from the 481 cases reported for 1992. For each year from 1975 through 1992, malaria cases in U.S. military personnel accounted for no more than 5% of reported cases. In 1993, however, malaria in U.S. military personnel accounted for 278 (22%) reported cases, representing an almost tenfold increase over the 29 cases reported for 1992.

Plasmodium *Species*

The *Plasmodium* species was identified in 1,216 (95%) of the 1,275 cases reported for 1993. *P. vivax* was identified from blood smears in 663 (52%) cases, representing a 43% increase from the 463 cases for 1992 (Table 2). The 457 (36%) *P. falciparum* cases identified during 1993 represented a 54% increase from the 296 cases reported for 1992. *P. malariae* and *P. ovale* were identified in 53 (4%) and 41 (3%) of cases, respectively. Two mixed infections were reported. The species was undetermined in 59 (5%) cases.

TABLE 1. Number of malaria cases* in U.S. and foreign civilians and U.S. military personnel — United States, 1966–1993

Year	U.S. military personnel	U.S. civilians	Foreign civilians	Unknown	Total
1966	621	89	32	22	764
1967	2,699	92	51	15	2,857
1968	2,567	82	49	0	2,698
1969	3,914	90	47	11	4,062
1970	4,096	90	44	17	4,247
1971	2,975	79	69	57	3,180
1972	454	106	54	0	614
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

*A case was defined as symptomatic or asymptomatic illness that occurs in the United States in a person who has microscopically 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.

Area of Acquisition and of Diagnosis

The number of malaria infections acquired in Africa during 1993 (745 [58%] cases) was more than twice the number of cases acquired there during 1992 (337 [37%] cases) (Table 3). Of cases reported for 1993, 259 (20%) cases had been acquired in Asia, representing a 22% decrease from the 330 (36%) cases for 1992.

In the United States, cases are reported by the state in which they are diagnosed (Figure 2). The number of cases reported from New York State (excluding New York

FIGURE 1. Number of malaria cases in U.S. and foreign civilians — United States,* 1967–1993[†]
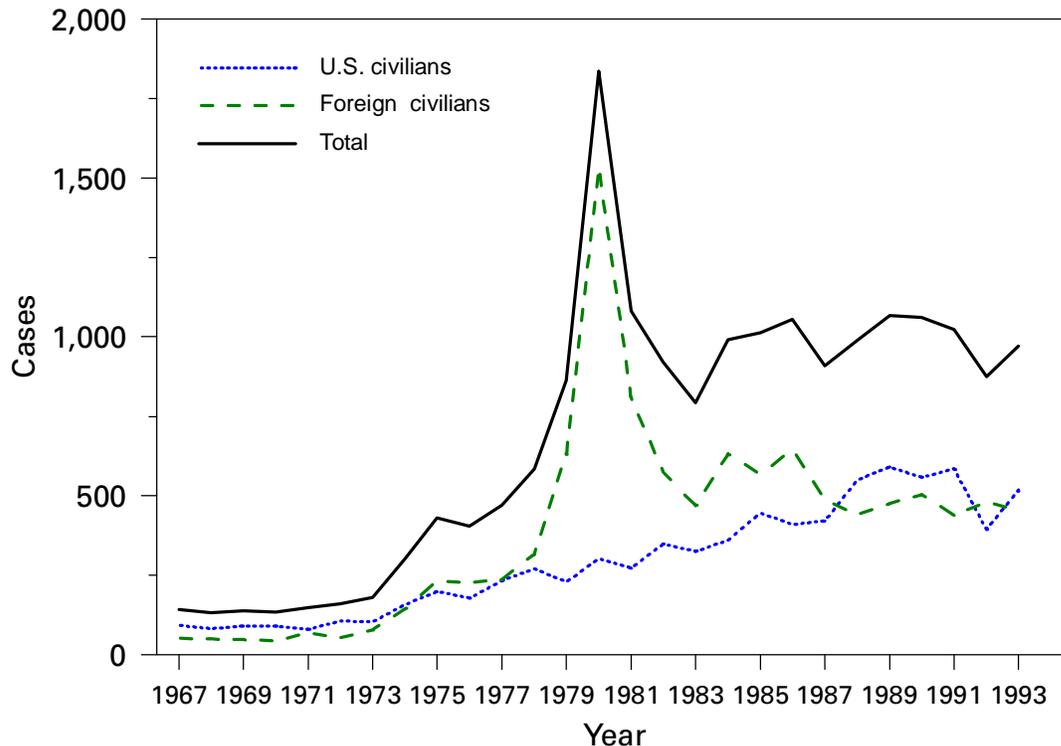
*Includes Puerto Rico, the Virgin Islands, and Guam.
[†]The large increase in the number of cases reported for 1980 primarily reflected cases diagnosed in immigrants from Southeast Asia after the Vietnam conflict.

TABLE 2. Number of malaria cases, by *Plasmodium* species — United States, 1992 and 1993

Plasmodium species	1992		1993	
	No.	(%)	No.	(%)
P. vivax	463	(50.9)	663	(52.0)
P. falciparum	296	(32.5)	457	(35.8)
P. malariae	39	(4.3)	53	(4.2)
P. ovale	28	(3.1)	41	(3.2)
Undetermined	84	(9.2)	59	(4.6)
Mixed	0	(0.0)	2	(0.2)
Total	**910**	**(100.0)**	**1,275**	**(100.0)**

City) increased from 77 in 1992 to 191 in 1993; this increase primarily reflected the 107 cases diagnosed in military personnel returning from Somalia. The number of cases in North Carolina decreased from 85 in 1992 to 42 in 1993; this decrease primarily reflected a decrease in the number of cases in Montagnard refugees arriving in the state. In addition, New York City began submitting case reports to CDC in 1993. One hundred thirty cases were reported from New York City for 1993, compared with one case for 1992.

Interval Between Arrival and Onset of Illness

Of those persons who became ill with malaria after arriving in the United States, the interval between the dates of arrival and the onset of illness was known for 847 persons. The species was not identified for 37 of the 847 cases, and one case was a mixed infection. Of the remaining 809 cases caused by a single infecting *Plasmodium* species, symptoms developed within 30 days after the person's arrival in the United States in 278 (88%) of 316 *P. falciparum* infections and in 84 (20%) of 431 *P. vivax* infections (Table 4). Nineteen (2%) of these 809 infected persons became ill >1 year after arrival in the United States. Another 58 persons reportedly became ill from 1 to 163 days before arrival in the United States. Thirty-six (62%) of these 58 persons became ill within a week before arrival in the United States.

FIGURE 2. Number of malaria cases, by state in which the disease was diagnosed* — United States, 1993
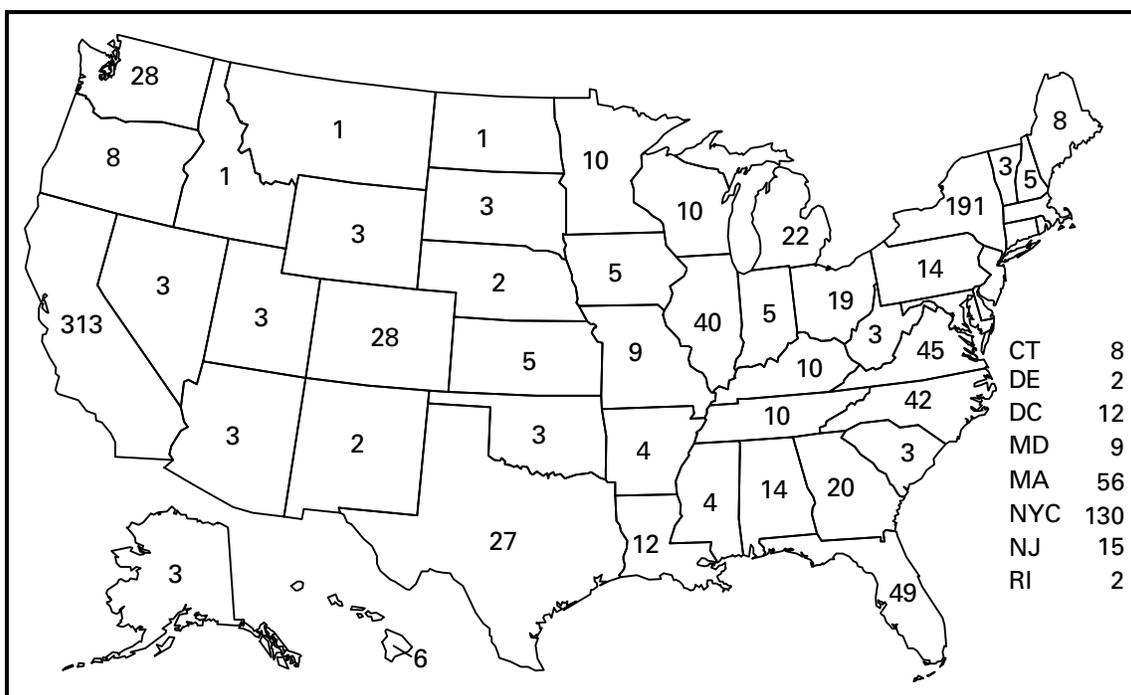
*Of the 1,275 malaria cases reported for 1993, only 11 cases had been acquired in the United States. Five of these cases had been acquired congenitally, and three had been acquired through transfusion of blood or blood products. Two cases probably were locally acquired, and one case probably resulted from a needlestick injury.

TABLE 3. Number of malaria cases, by *Plasmodium* species and area of acquisition — United States, 1993

Area of acquisition	*P. vivax*	*P. falciparum*	*P. malariae*	*P. ovale*	Mixed	Unknown	Total
AFRICA	**256**	**376**	**39**	**36**	**0**	**38**	**745**
Algeria	0	0	0	0	0	0	0
Angola	0	1	0	0	0	0	1
Benin	0	0	0	1	0	0	1
Burkina Faso	0	1	0	0	0	0	1
Cameroon	0	11	0	4	0	1	16
Central African Republic	0	2	1	0	0	0	3
Chad	0	1	0	0	0	0	1
Congo	0	1	0	0	0	0	1
Djibouti	0	0	0	0	0	0	0
Egypt	0	0	0	0	0	0	0
Equatorial Guinea	0	0	0	0	0	0	0
Ethiopia	5	2	0	0	0	0	7
Gambia	0	0	1	0	0	0	1
Ghana	1	36	0	3	0	6	46
Guinea	1	0	0	0	0	0	1
Guinea-Bissau	0	1	1	0	0	0	2
Ivory Coast	1	21	1	0	0	0	23
Kenya	6	20	5	3	0	0	34
Liberia	2	12	1	2	0	0	17
Madagascar	2	1	0	0	0	0	3
Malawi	0	1	0	2	0	1	4
Mali	0	7	0	0	0	0	7
Mauritania	0	0	0	0	0	0	0
Mozambique	0	0	0	1	0	0	1
Niger	0	0	0	0	0	1	1
Nigeria	3	135	11	8	0	11	168
Rwanda	0	1	0	0	0	0	1
Senegal	0	10	0	0	0	0	10
Sierra Leone	0	22	3	2	0	2	29
Somalia	216	12	2	1	0	7	238
South Africa	0	0	0	0	0	0	0
Sudan	5	12	1	0	0	1	19
Tanzania	0	4	0	0	0	0	4
Togo	0	3	0	0	0	1	4
Uganda	3	8	0	4	0	1	16
Zaire	0	1	2	0	0	0	3
Zambia	1	2	0	0	0	0	3
Zimbabwe	0	1	0	0	0	1	2
Africa, Central*	1	0	0	1	0	0	2
Africa, East*	5	14	2	1	0	1	23
Africa, South*	1	5	0	0	0	0	6
Africa, West*	1	17	3	1	0	1	23
Africa, Unspecified*	2	11	5	2	0	3	23
ASIA	**214**	**28**	**2**	**2**	**0**	**13**	**259**
Afghanistan	0	0	0	0	0	0	0
Bangladesh	3	0	0	0	0	0	3
Cambodia	0	0	0	0	0	1	1
China	0	0	0	0	0	0	0
India	154	16	0	1	0	9	180
Indonesia	11	1	0	0	0	2	14
Laos	1	2	0	0	0	1	4

TABLE 3. Number of malaria cases, by *Plasmodium* species and area of acquisition — United States, 1993 — Continued

Area of acquisition	*Plasmodium* species						Total
	P. vivax	*P. falciparum*	*P. malariae*	*P. ovale*	Mixed	Unknown	
ASIA (cont'd)							
Malaysia	0	0	0	0	0	0	0
Myanmar (Burma)	1	0	0	0	0	0	1
Nepal	1	0	0	0	0	0	1
Pakistan	15	2	0	0	0	0	17
Philippines	3	0	0	0	0	0	3
Saudi Arabia	1	0	0	0	0	0	1
Sri Lanka	1	0	0	0	0	0	1
Thailand	3	1	1	0	0	0	5
Vietnam	10	1	1	1	0	0	13
Yemen	0	1	0	0	0	0	1
Asia, Southeast*	3	2	0	0	0	0	5
Asia, Unspecified*	7	1	0	0	0	0	8
Middle East, Unspecified*	0	1	0	0	0	0	1
CENTRAL AMERICA AND CARIBBEAN	**106**	**30**	**5**	**1**	**2**	**2**	**146**
Belize	7	0	0	0	0	1	8
Caribbean, Unspecified*	0	0	1	0	0	0	1
Costa Rica	2	0	0	0	0	0	2
Dominican Republic	2	0	0	0	0	0	2
El Salvador	9	0	0	0	0	0	9
Guatemala	19	3	2	1	1	0	26
Haiti	0	20	0	0	0	0	20
Honduras	40	3	0	0	0	1	44
Nicaragua	10	1	0	0	1	0	13
Panama	0	0	1	0	0	0	0
Central America, Unspecified*	17	3	1	0	0	0	21
NORTH AMERICA	**16**	**5**	**1**	**0**	**0**	**1**	**23**
Mexico	10	1	1	0	0	1	13
United States	6	4	0	0	0	0	10
SOUTH AMERICA	**14**	**4**	**1**	**0**	**0**	**0**	**19**
Brazil	2	0	0	0	0	0	2
Colombia	1	0	0	0	0	0	1
Ecuador	2	0	0	0	0	0	2
French Guiana	0	0	0	0	0	0	0
Guyana	1	3	1	0	0	0	5
Venezuela	6	1	0	0	0	0	7
South America, Unspecified*	2	0	0	0	0	0	2
OCEANIA	**35**	**1**	**1**	**2**	**0**	**3**	**42**
Papua New Guinea	30	1	1	2	0	2	36
Solomon Islands	3	0	0	0	0	1	4
Vanuatu	0	0	0	0	0	0	0
Oceania, Unspecified*	2	0	0	0	0	0	2
Unknown	22	13	4	0	0	2	41
Total	**663**	**457**	**53**	**41**	**2**	**59**	**1,275**

*Country unspecified.

Imported Malaria Cases

Imported Malaria in Military Personnel

For 1993, 278 reported cases of imported malaria occurred in U.S. military personnel. Of these cases, 161 (58%) occurred in personnel of the U.S. Army; 100 (36%), the U.S. Marine Corps; and nine (3%), the U.S. Air Force. Eight (3%) cases occurred in military personnel for whom the service branch was not identified.

Of the total 278 cases, 234 (84%) were acquired in Somalia during Operation Restore Hope (8). *P. vivax* was the infecting species in 215 (92%) of these 234 cases, all of which were considered relapse infections; *P. falciparum* was the infecting species in 10 (4%) cases. Of the remaining 44 (16%) cases reported in U.S. military personnel, 20 had been acquired in Honduras.

Imported Malaria In Civilians

Of the 961 imported malaria cases in civilians, 508 (53%) were diagnosed in U.S. residents and 453 (47%) were in residents of other countries (Table 5). Of the 508 imported malaria cases in U.S. civilians, 276 (54%) occurred in persons who had traveled in Africa, representing a 45% increase over the 190 cases acquired in this region during 1992. Ninety-five (34%) of the 276 U.S. civilians who acquired malaria in Africa

TABLE 4. Number of imported malaria cases, by *Plasmodium* species and by interval between date of arrival in the country and onset of illness — United States, 1993

Interval (mos)	*Plasmodium* species								Total	
	P. vivax		*P. falciparum*		*P. malariae*		*P. ovale*			
	No.	(%)	No.	(%)	No.	(%)	No.	(%)	No.	(%)
0– 29	84	(19.5)	278	(88.0)	17	(51.5)	9	(31.0)	388	(48.0)
30– 89	127	(29.5)	32	(10.1)	8	(24.2)	5	(17.2)	172	(21.3)
90–179	107	(24.8)	1	(0.3)	5	(15.2)	8	(27.6)	121	(15.0)
180–364	98	(22.7)	3	(0.9)	2	(6.1)	6	(20.7)	109	(13.5)
≥365	15	(3.5)	2	(0.6)	1	(3.0)	1	(3.4)	19	(2.3)
Total	**431**	**(100.0)**	**316**	**(100.0)**	**33**	**(100.0)**	**29**	**(100.0)**	**809**	**(100.0)**

TABLE 5. Number of imported malaria cases in U.S. and foreign civilians, by area of acquisition — United States, 1993

Area of acquisition	U.S. civilians		Foreign civilians		Total	
	No.	(%)	No.	(%)	No.	(%)
Africa	276	(54.3)	213	(47.0)	489	(50.9)
Asia	91	(17.9)	157	(34.7)	248	(25.8)
Caribbean	11	(2.2)	12	(2.6)	23	(2.4)
Central America	54	(10.6)	46	(10.2)	100	(10.4)
Mexico	5	(1.0)	7	(1.5)	12	(1.2)
Oceania	38	(7.5)	2	(0.4)	40	(4.2)
South America	17	(3.3)	2	(0.4)	19	(2.0)
Unknown	16	(3.1)	14	(3.1)	30	(3.1)
Total	**508**	**(100.0)**	**453**	**(100.0)**	**961**	**(100.0)**

reported having traveled in Nigeria, and 100 (36%) had traveled in other parts of West Africa. Of the 453 cases of imported malaria in foreign civilians during 1993, 213 (47%) had been acquired in Africa; in comparison, 142 cases had been acquired in Africa during 1992. The 157 (35%) cases of imported malaria acquired during 1993 in Asia by foreign civilians represented a 33% decrease from the 233 cases acquired in Asia during 1992.

Use of Antimalarial Chemoprophylaxis

Information concerning use of chemoprophylaxis was available for 482 (95%) of the 508 U.S. civilians who had imported malaria. Of these 482 persons, 229 (48%) had not taken chemoprophylaxis, 116 (24%) had not taken a drug recommended by CDC for the area visited, and 28 (6%) did not specify the type of chemoprophylaxis taken (*9*). The remaining 109 (23%) persons reported having taken a medication recommended by CDC for the area visited; however, 23 (21%) of these persons had not taken the recommended dosage, and information was incomplete for 18 (17%). Fifty-seven (52%) of these 109 cases were clinically consistent with relapses of *P. vivax* or *P. ovale* infection.

The remaining 11 cases occurred in persons who reported having been compliant with a regimen of mefloquine. Of these 11 cases, five were diagnosed as *P. falciparum* infection, three cases of which had been acquired in West Africa. Serum levels of mefloquine were measured on four of the five persons infected with *P. falciparum*, and none had mefloquine levels adequate to provide protection from blood-stage infection (*10*). Illnesses in the remaining six persons who had been compliant with a regimen of mefloquine were diagnosed as *P. malariae* infection 1–2 months after completion of chemoprophylaxis.

The purpose of travel to foreign countries with known malaria transmission was reported for 303 (60%) of the 508 U.S. civilians who had imported malaria (Table 6). Of these 303 persons, 63 (21%) had traveled to visit friends and relatives, 61 (20%) had been tourists, and 56 (18%) had been conducting missionary work.

TABLE 6. Number of imported malaria cases in U.S. civilians, by purpose of travel at the time of acquisition — United States, 1993

Category	Imported cases	
	No.	**(%)**
Business representative	41	(8.1)
Government employee	6	(1.2)
Missionary	56	(11.0)
Peace Corps volunteer	9	(1.8)
Teacher/Student	48	(9.4)
Tourist	61	(12.0)
Visiting a friend or relative	63	(12.4)
Other	19	(3.7)
Unknown	205	(40.4)
Total	**508**	**(100.0)**

Malaria Acquired in the United States

Congenital Malaria

The following five cases of congenital malaria were reported for 1993.

Case 1. On January 6, 1993, a 3-week-old girl was admitted to a hospital in California because of fever. An examination of the infant's peripheral blood smear demonstrated the presence of *P. vivax* parasites. She was successfully treated with chloroquine. The infant also received primaquine, although congenital infection does not result in liver stage infection and, therefore, does not require such treatment for radical cure.

The infant's mother, a resident of Tijuana, Mexico, had traveled in Guatemala from December 1991 through January 1992. She had treated herself with an unknown medication for malaria while in Guatemala. On December 21, 1992, while visiting in California, she was admitted to a hospital, where she was diagnosed as having *P. vivax* malaria and treatment with chloroquine was initiated. The infant was born on December 22. After the delivery, the mother was treated with primaquine.

Case 2. In June 1993, an 18-day-old boy was admitted to a hospital in California because of fever, anemia, and thrombocytopenia. An examination of the infant's blood smears demonstrated the presence of *P. vivax*. The symptoms and parasitemia resolved after treatment with chloroquine.

The infant's mother had arrived recently from Guatemala, where she had been treated for malaria during the first and seventh months of this pregnancy but had not received chemoprophylaxis for prevention of relapses during the remainder of the pregnancy. Blood smears obtained from the mother after diagnosis of the infant's infection reportedly demonstrated a dual infection with *P. vivax* and *P. malariae*; however, the slides were not provided to CDC for confirmation. The mother was treated with chloroquine, but her medical records did not indicate whether she also was treated with primaquine.

Case 3. On July 12, 1993, a 7-week-old girl was admitted to a hospital in Florida because of fever, irritability, splenomegaly, anemia, and thrombocytopenia. *P. falciparum* infection was diagnosed after examination of the infant's blood smear, and she was treated with quinine and pyrimethamine-sulfadoxine. Medical information concerning the infant's mother, who had resided recently in Sierra Leone, was not available.

Case 4. During September 1993, a 3-week-old girl was admitted to a hospital in California because of fever. Parasites consistent with *P. vivax* were present on examination of thick and thin blood smears. The infant was treated with chloroquine and subsequently had resolution of fever and clearance of parasitemia.

Symptoms of malaria did not develop in the infant's twin. The infants' mother had traveled from India 11 months before the delivery, and she reported having had febrile episodes during the pregnancy. Indirect immunofluorescent antibody (IFA) assays were performed on serum samples obtained from the mother and both twins. IgG and IgM titers to *P. vivax* for the parasitemic infant were 1:4,096 and 1:1,024, respectively. Both the mother and the asymptomatic twin had high titers of serum IgG (1:1,024) but

low titers of IgM (1:16 in the mother and <1:16 in the asymptomatic twin) to *P. vivax*. The mother was treated with chloroquine and primaquine, and the asymptomatic twin was not treated.

Case 5. During November 1993, a 7-week-old girl was admitted to a hospital in Texas because of fever. An examination of her blood smear demonstrated the presence of parasites consistent with *P. vivax*. The child was treated with chloroquine, and the symptoms and parasitemia resolved.

The child had been delivered by cesarean section because of abruptio placentae. The mother had emigrated from India in January 1993 and had been treated for an unspecified type of malaria at 4 months' gestation; she reported no recurrent fevers during her pregnancy. The mother's blood smears were negative for parasites. Treatment information on the mother was unavailable.

Cryptic Malaria

The following three cases of cryptic malaria were reported for 1993.

Cases 1 and 2. The first case occurred in a 27-year-old man who was admitted on both July 20 and August 5, 1993, to a hospital in New York City; both hospitalizations were for fever of unknown origin. On August 17, an examination of smears of a bone marrow aspirate demonstrated the presence of parasites consistent with *P. falciparum*.

The second case occurred in a 22-year-old woman who was admitted to another hospital in New York City on July 21, 1993, because of fever of unknown origin. On August 4, her illness was diagnosed as malaria after an examination of her peripheral blood smear demonstrated the presence of *P. falciparum* parasites.

The man had emigrated from Poland in May 1993 but reported never having traveled to a country with known malaria transmission. The woman had never traveled outside the United States. Neither person had ever received a blood transfusion, used injection drugs, or sustained a needlestick injury. These two persons resided within 2 miles of each other.

The New York City Department of Health and CDC (*11*) investigated both cases and determined that the two patients probably acquired malaria in New York City through mosquito-borne transmission. In addition, a 17-year-old woman who lived within 2 miles of the first two patients was diagnosed on August 4 as having *P. falciparum* malaria. This case was investigated as a possible case of local mosquito-borne infection; however, the infection was classified as imported malaria because the woman had traveled to Thailand during July 1991.

Case 3. On March 29, 1993, fever developed in a 34-year-old woman 2 weeks after she sustained a needlestick injury in the medical office where she was employed. The woman did not seek medical care until April 5, when an examination of her blood smears demonstrated the presence of *P. falciparum* parasites (8% of her red blood cells were infected). She was treated initially with 1.25 g of mefloquine, 600 mg of quinine, and 900 mg of clindamycin, followed by 250 mg of mefloquine daily for the next 3 days. On April 8, she complained of right upper quadrant pain of unclear etiology, and treatment for malaria was resumed with oral quinine sulfate. She died the next day.

The needlestick injury involved a syringe that had been used to obtain blood from a patient who had arrived recently from Africa; blood smears obtained from this patient were reportedly negative for parasites but were unavailable for review by CDC. The woman had traveled several months before to Tijuana and Acapulco, Mexico, which are not considered to be areas with known malaria transmission. She also had traveled in Africa 5 years earlier. Because malarial symptoms developed in the woman within 2 weeks after she sustained the needlestick injury and because she had not traveled recently to an area in which malaria is endemic, the infection could have resulted from the injury; however, a definitive conclusion regarding the source of infection could not determined.

Induced Malaria

Case 1. In January 1993, illness in a 78-year-old man who had large cell lymphoma was diagnosed at a Connecticut hospital as *P. vivax* infection. He had never traveled outside the United States, but he had received multiple transfusions of blood and blood products from 63 different donors. On the basis of the results of a survey questionnaire mailed to 59 of these donors, the 29 donors who had ever traveled to an area in which malaria is endemic were tested serologically.

One platelet donor had a serum IFA assay titer of 1:256 to *P. falciparum*, 1:64 to *P. vivax,* 1:64 to *P. ovale*, and <1:16 to *P. malariae* on blood obtained on August 31, 1993. An examination of this donor's blood smears demonstrated the presence of *P. falciparum* parasites. This donor had been born in India, and the last time he had visited there before the platelet donation was in 1987. He again visited India from May through July 1993 (i.e., between the time of the donation and the investigation of this case). Repeat serologic testing on October 14 demonstrated an IFA assay titer of 1:64 for *P. falciparum* and 1:16,384 for *P. vivax,* the latter of which was consistent with recent *P. vivax* infection. An examination of blood smears at that time did not demonstrate the presence of parasites. The donor was treated for both *P. vivax* and *P. falciparum* infection. Whether this donor was the source of the recipient's infection is uncertain, because the donor might have acquired malaria during his most recent trip to India.

Case 2. On December 21, 1992, a 62-year-old man who had multiple myeloma was admitted to a hospital in New York City because of fever. He was treated initially for presumptive bacterial sepsis, but he continued to have febrile episodes. On January 7, 1993, a bone marrow aspirate was performed, and malaria parasites were identified on microscopic examination. Subsequent examination of his peripheral blood smear confirmed the diagnosis of *P. falciparum* infection, with a 12% level of parasitemia. He was treated with intravenous quinidine and tetracycline with subsequent resolution of fever and parasitemia.

The patient had been born in Russia and had moved to the United States 10 years before the diagnosis of malaria. Two years before the diagnosis, he had vacationed in Cancun, Mexico, although this is not an area with known malaria transmission. He had received two units of packed red blood cells on November 22, 1992, and one unit of packed red blood cells 7 days later. All three of the blood donors were subsequently tested for malaria antibodies; a serum sample from one of these donors had a positive reaction, with an IFA assay titer of >1:16,384 for *P. falciparum* malaria. The implicated

donor was a man who had been born in Nigeria and who had been to both Nigeria and Haiti during September 1992; however, he had not reported this information to the blood bank at the time of the donation. An examination of blood smears obtained from the donor demonstrated parasites consistent with *P. falciparum.* He was treated with quinine sulfate and pyrimethamine-sulfadoxine.

Case 3. In December 1993, a 60-year-old woman who had received a liver transplant the previous month was diagnosed as having *P. vivax* infection. She was treated successfully with chloroquine and primaquine. She had been born in the United States and had never traveled to an area in which malaria is endemic. She had received 110 units of blood and blood products during her hospitalization for the liver transplantation. Serum was obtained from the liver donor and all donors from whom she had received red blood cells and platelets. Only one platelet donor had detectable antibodies for *Plasmodium*.

The implicated donor was a woman who had emigrated from Ghana in 1990; she had not traveled out of the United States since her arrival. She was asymptomatic at the time of donation. IFA assay titers of her serum were 1:1,024 for *P. ovale,* 1:1,024 for *P. malariae*, 1:4,096 for *P. falciparum*, and 1:256 for *P. vivax*, a pattern consistent with that of a person from a geographic area in which the incidence of malaria transmission is high. An examination of blood smears obtained from this donor demonstrated rare ring forms consistent with *Plasmodium* infection, but a definitive species identification was not possible.

Another person had received red blood cells from this donor. An IFA assay of this recipient's serum only identified antibodies to *P. ovale* (titer 1:64), and an examination of this recipient's blood smear did not demonstrate the presence of parasites. This recipient was treated with chloroquine, and the donor was treated with chloroquine and primaquine. A DNA amplification using polymerase chain reaction of blood samples obtained from the donor and the first recipient (i.e., the person with the initially diagnosed infection) identified the infecting species as *P. ovale*, thus highlighting the limitations of using parasite morphology for species identification—particularly when differentiating *P. vivax* and *P. ovale*.

Deaths Attributed to Malaria

The following eight deaths were attributed to malaria during 1993.

Case 1. A 32-year-old woman in her 35th week of pregnancy came to the United States from Liberia on March 13, 1993. She had had an illness that was diagnosed as malaria in June 1992, for which she was treated with chloroquine and pyrimethamine. Her pregnancy was complicated by preeclampsia. Two days after arrival in the United States, she became ill with myalgia and fever (103 F). She was hospitalized on March 20. An examination of her blood smear demonstrated the presence of parasites consistent with *P. falciparum*, and treatment with oral quinine sulfate was initiated. On March 21, adult respiratory distress syndrome and hypoglycemia developed in the woman. Two days later, pyrimethamine-sulfadoxine was included in her treatment regimen. Because her respiratory status was deteriorating rapidly, a cesarean section was performed on March 23. The woman's respiratory status continued to worsen, and she died on March 30.

The woman's infant girl weighed 2.5 kg and was apparently healthy. Although an examination of placental sections demonstrated the presence of *P. falciparum* parasites, no parasites were demonstrated on blood smears obtained from the infant on March 24.

Case 2. On April 17, 1993, a 51-year-old woman returned from traveling in South Africa and Zimbabwe. She had taken chloroquine for antimalarial chemoprophylaxis while traveling. Fever developed in the woman on April 24, and an examination of the woman's blood smear on April 26 demonstrated the presence of *P. falciparum* parasites. She was treated with a single dose of 1.5 g of mefloquine on April 27. She continued to have febrile episodes; on April 30, she complained of intense left ear pain and was leukopenic (white blood cell count of 2000/mm^3). Doxycycline and norfloxacin were added to her treatment regimen for additional coverage against *P. falciparum* and bacterial pathogens. The patient had a cardiac arrest and died on April 31.

Case 3. A 24-year-old male U.S. resident was working as a volunteer in the jungles of Guyana. He had not been taking antimalarial chemoprophylaxis. On March 29, 1993, he was hospitalized in Guyana because of fever. Detailed information concerning this hospitalization was unavailable. He was airlifted to a hospital in Miami on April 5, at which time he had altered mental status. He died within an hour after his arrival. A postmortem examination indicated cerebral malaria caused by *P. falciparum* infection.

Case 4. On November 11, 1993, a 51-year-old woman returned from a 2-week visit to Nigeria, where she had taken hydroxychloroquine as antimalarial chemoprophylaxis. Fever developed in the woman on November 17, and she was hospitalized the next day. A blood smear obtained from the woman was examined and reported to be negative for parasites. On November 21, she became lethargic and had lactic acidosis. She was transferred to another hospital on November 22, at which time she had altered mental status consistent with cerebral malaria. An examination of her blood smear demonstrated the presence of *P. falciparum* parasites (4% of her red blood cells were infected). Treatment with intravenous quinidine and oral pyrimethamine-sulfadoxine was initiated at the time of admission. During her hospitalization, she was diagnosed with adult respiratory distress syndrome and required mechanical ventilation. She subsequently acquired nosocomial bacterial pneumonia. She died as a result of respiratory failure on December 15.

Case 5. In June 1993, a 63-year-old female native of India traveled to the United States. She had had multiple episodes of malaria that had been treated in India. On August 8, she was admitted to a hospital in Missouri because of fever (100.5 F), nausea, vomiting, and diarrhea. An examination of her blood smears reportedly demonstrated a mixed *Plasmodium* infection, and she was treated with oral quinine sulfate and doxycycline. The symptoms of her illness improved markedly, and she was discharged 2 days after admission. On August 14, after she had completed a 3-day course of quinine and was on her fourth day of treatment with doxycycline, she was admitted to another hospital because of shortness of breath that required mechanical ventilation. A radiograph of her chest was consistent with pulmonary edema, and an echocardiogram demonstrated diffuse cardiac dysfunction consistent with

myocarditis or ischemia. Her cardiac enzymes were normal, excluding the diagnosis of acute myocardial infarction. The patient died as a result of congestive heart failure. Subsequent reexamination by CDC of the initial blood smears from the first hospitalization demonstrated the presence of only *P. vivax* parasites (1.3% of her red blood cells were infected). The underlying cause of myocardial disease was not determined.

Case 6. On January 10, 1993, a 67-year-old woman was admitted to a hospital in Florida because of febrile episodes. An examination of her blood smears demonstrated the presence of *P. falciparum* parasites. She was treated with quinine sulfate. During her hospitalization, she was diagnosed with adult respiratory distress syndrome and cardiac arrhythmia, the latter of which caused her death on January 20. The arrhythmia may have resulted from either *P. falciparum*-associated myocardial dysfunction or an adverse reaction to quinine.

Case 7. On January 1, 1993, fever developed in a 30-year-old man 1 day after he returned from a trip to Nigeria. He had not taken antimalarial chemoprophylaxis while traveling. He was hospitalized on January 20 because of headache, nausea, and vomiting. His illness was diagnosed initially as viral meningitis, but a subsequent examination of his blood smears identified *P. falciparum* parasitemia. Treatment with quinine and pyrimethamine-sulfadoxine was initiated. He also was diagnosed as having bacterial pneumonia, which was treated with a cephalosporin antibiotic, and mild renal insufficiency. His temperature decreased with treatment. On January 24, the patient signed out of the hospital against medical advice without completing his prescribed course of quinine. On February 1, he was admitted to another hospital because of respiratory distress. An examination of his blood smears again demonstrated the presence of *P. falciparum* parasites, and findings on his chest radiograph were consistent with adult respiratory distress syndrome. He was treated with intravenous quinidine, pyrimethamine-sulfadoxine, and clindamycin. His respiratory status did not improve, and he died on February 6.

Case 8. See Cryptic Case #3.

DISCUSSION

The 1,275 cases of malaria reported to CDC for 1993 represented a 40% increase from the 910 cases reported for 1992 (*7*). This increase was attributed primarily to two events. First, the number of cases in military personnel increased almost tenfold, reflecting the 234 cases of malaria acquired in Somalia during Operation Restore Hope (which occurred from December 1992 through May 1993) (*8*). This increase represented the largest number of malaria cases in military personnel in 1 year since the peak in cases associated with the return of troops from Vietnam. Second, during 1993, the New York City Department of Health began routinely sending all malaria case report forms to CDC, reporting 130 cases for that year.

In comparison with 1992, the number of *P. falciparum* infections reported for 1993 in U.S. civilians returning from Africa increased by 45%; this overall increase primarily reflected the increased number of cases acquired in Nigeria and other parts of West Africa. Almost all these cases occurred in persons who had not taken a chemoprophylactic regimen recommended by CDC.

Failure to take the appropriate antimalarial chemoprophylaxis and noncompliance with dosing regimens contributed to most of the imported malaria cases in U.S. civilians during 1993. Only 25% of U.S. civilians diagnosed with malaria had taken an appropriate chemoprophylactic medication recommended by CDC for their area of travel. The drug recommended by CDC for travelers to areas with known transmission of chloroquine-resistant *P. falciparum* is mefloquine (*9*). Excluding cases of relapse infection and cases for which information was incomplete, symptomatic parasitemia developed in only 11 patients who had correctly taken mefloquine for chemoprophylaxis. Serum mefloquine levels were found to be below a protective level for all four of the five patients with *P. falciparum* infection who were tested. This may indicate noncompliance or differences in metabolism of mefloquine in these persons (*10*). The remaining six patients had *P. malariae* parasitemia >2 months after completion of their chemoprophylactic regimen.

Health-care providers should contact CDC if chemoprophylaxis failure is suspected, thus enabling measurement of serum levels of the chemoprophylactic agent. The development of malarial infection in the setting of protective levels of mefloquine might indicate the emergence of mefloquine-resistant strains of the parasite. Reported cases of chloroquine-resistant *P. falciparum* infections in travelers returning from Africa prompted CDC to revise the recommended antimalarial chemoprophylaxis for travelers to that region (*5*).

The signs and symptoms of malarial illness are variable, but most patients experience fever. Other symptoms include headache, back pain, chills, increased sweating, myalgia, nausea, vomiting, diarrhea, and cough. The diagnosis of malaria should be considered for any person who has these symptoms and who has traveled to an area in which malaria is transmitted. Malaria also should be considered in the differential diagnosis of persons who have a fever of unknown origin, regardless of their travel history. Asymptomatic parasitemia can occur among long-term residents of areas in which malaria is endemic. Untreated *P. falciparum* infection can progress to coma, renal failure, pulmonary edema, and death.

During 1993, eight (0.7%) persons who had malaria died. Previously described factors that may have contributed to these deaths included failure to take the recommended antimalarial chemoprophylaxis during travel, delay in seeking medical care, delay in diagnosis and initiation of therapy, and use of suboptimal treatment regimens (*12*). None of the patients who died during 1993 had taken the appropriate chemoprophylaxis. Failure to identify and aggressively treat major complications also may have contributed to some of these deaths.

Treatment for malaria should be initiated immediately after the diagnosis has been confirmed by a positive blood smear. Treatment should be determined on the basis of the infecting *Plasmodium* species, the parasite density, and the patient's clinical status (*10*). Although non-*falciparum* malaria rarely causes severe illness, persons diagnosed as having *P. falciparum* infection are at risk for developing severe life-threatening complications. The use of intravenous quinidine gluconate and exchange transfusion might be necessary to manage patients who have high levels of parasitemia or severe complications (*13*).

Two malaria cases that occurred in New York City were probably locally acquired from infected *Anopheles* sp. mosquitoes; these cases represented the seventh outbreak of locally acquired infection in the continental United States during 1989–1993

(*11*). Local outbreaks were identified twice in San Diego County in 1989 and once in 1990, once in rural Florida in 1990, and twice in suburban New Jersey in 1991 (*2–4*). The outbreak in 1993 differs from other recent outbreaks in that a) it occurred in an urban setting and b) the infecting organism was *P. falciparum.* Health-care providers should consider malaria in the differential diagnosis of any patient who has an unexplained fever, regardless of the patient's travel history, and they should conduct a blood smear examination if indicated. To enable prompt investigation of malaria cases in patients who have not traveled to an area in which malaria is endemic, health-care providers should immediately notify their state or local health department and CDC of such cases.

Health-care providers are encouraged to consult appropriate sources for malaria treatment recommendations or call CDC's National Center for Infectious Diseases, Division of Parasitic Diseases at (770) 488-7760 (*10*). Detailed recommendations for preventing malaria are available 24 hours a day from the CDC Malaria Hotline, which can be accessed by telephone ([404] 332-4555), facsimile ([404] 332-4565), or CDC's World-Wide Web server (http://www.cdc.gov/). CDC annually publishes updated recommendations in the *Health Information for International Travel* (*9*), which is available through the Superintendent of Documents, U.S. Government Printing Office, Washington, DC 20402-9235; telephone (202) 512-1800.

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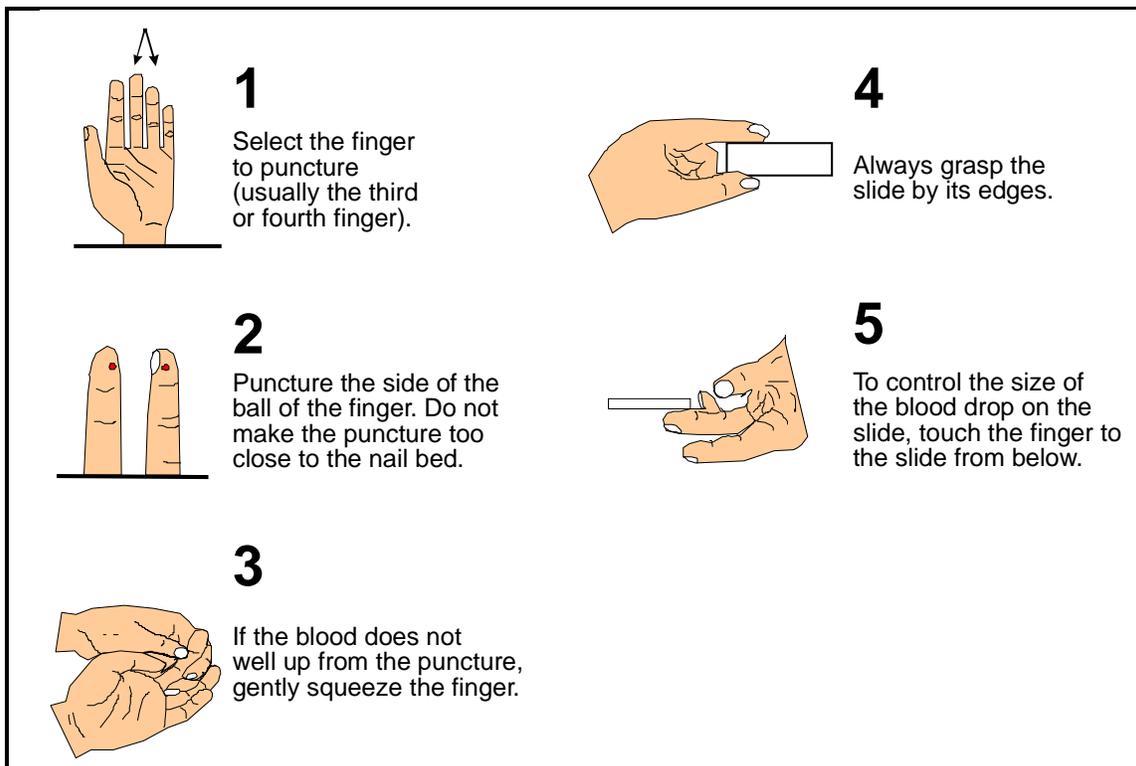
APPENDIX

Microscopic Procedures for Diagnosing Malaria

To establish the diagnosis of malaria, a blood smear must be prepared from fresh finger-prick blood (Figures A-1 and A-2).* The thin smear is fixed in methanol before staining; the thick smear is stained unfixed. Many hospitals have a Wright-Giemsa stain available, which is acceptable; however, Wright stain alone will not reliably stain *Plasmodium* parasites. For best results, the smear should be stained with a 3% Giemsa solution (pH of 7.2) for 30–45 minutes. In *P. falciparum* infections, the parasite density should be estimated by counting the percentage of red blood cells infected—not the number of parasites—under an oil immersion on a thin film.

Thick blood smears are more sensitive in detecting malaria parasites because the blood is concentrated, allowing a greater volume of blood to be examined. However, thick smears are more difficult to read, and thin smears may be preferred by laboratories that have limited experience. *Plasmodium* parasites are always intracellular, and

FIGURE A-1. Blood collection for thin or thick blood film

1 Select the finger to puncture (usually the third or fourth finger).

2 Puncture the side of the ball of the finger. Do not make the puncture too close to the nail bed.

3 If the blood does not well up from the puncture, gently squeeze the finger.

4 Always grasp the slide by its edges.

5 To control the size of the blood drop on the slide, touch the finger to the slide from below.
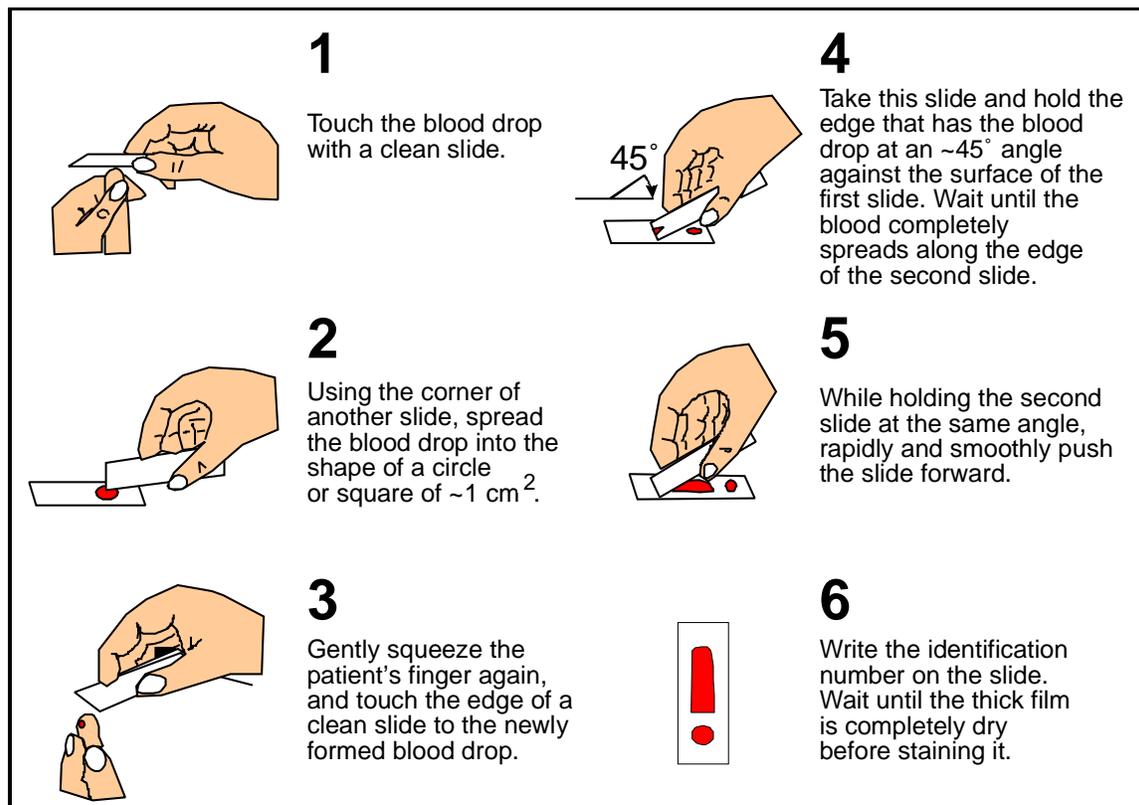
they demonstrate, if stained correctly, blue cytoplasm with a red chromatin dot. Common errors in reading malaria smears are caused by platelets overlying a red blood cell, concern about missing a positive slide, and misreading artifacts as parasites. Persons suspected of having malaria but whose blood smears do not demonstrate the presence of parasites should have blood smears repeated approximately every 12–24 hours for 3 consecutive days. If smears remain negative, then the diagnosis of malaria is unlikely.

For rapid diagnosis, make the thick and thin films on separate slides. Air dry the thin film, fix it with methyl alcohol, and immediately stain it. If no parasites are found on the thin film, wait until the thick film is dry and examine it for organisms that may not have been detected on the thin preparation.

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*In Figures A-1 and A-2, the hands are shown ungloved to better illustrate their placement during the procedures. However, wearing gloves while processing blood specimens is recommended to prevent transmission of bloodborne pathogens (*MMWR* 1988;37:377–82, 387–8 and *MMWR* 1987;36[no. S2]).

FIGURE A-2. Preparation of a thin and thick blood film on the same slide

1 Touch the blood drop with a clean slide.

2 Using the corner of another slide, spread the blood drop into the shape of a circle or square of ~1 cm^2.

3 Gently squeeze the patient's finger again, and touch the edge of a clean slide to the newly formed blood drop.

4 Take this slide and hold the edge that has the blood drop at an ~45° angle against the surface of the first slide. Wait until the blood completely spreads along the edge of the second slide.

5 While holding the second slide at the same angle, rapidly and smoothly push the slide forward.

6 Write the identification number on the slide. Wait until the thick film is completely dry before staining it.

State and Territorial Epidemiologists and Laboratory Directors

State and Territorial Epidemiologists and Laboratory Directors are acknowledged for their contributions to *CDC Surveillance Summaries*. The epidemiologists listed below were in the positions shown as of December 1996, and the laboratory directors listed below were in the positions shown as of December 1996.

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Alaska	John P. Middaugh, MD	Gregory V. Hayes, DrPH
Arizona	Robert W. England, Jr., MD, MPH	Barbara J. Erickson, PhD
Arkansas	Thomas C. McChesney, DVM	Michael G. Foreman
California	Stephen H. Waterman, MD, MPH	Michael G. Volz, PhD
Colorado	Richard E. Hoffman, MD, MPH	Robert Quillan, MS, MSPH
Connecticut	James L. Hadler, MD, MPH	Sanders F. Hawkins, PhD
Delaware	A. LeRoy Hathcock, PhD	Chris Zimmerman, MA (Acting)
District of Columbia	Martin E. Levy, MD, MPH	James B. Thomas, ScD
Florida	Richard S. Hopkins, MD, MSPH	E. Charles Hartwig, ScD
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Idaho	Jesse F. Greenblatt, MD, MPH	Richard H. Hudson, PhD
Illinois	Byron J. Francis, MD, MPH	David F. Carpenter, PhD
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Kansas	Gianfranco Pezzino, MD, MPH	Roger H. Carlson, PhD
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Louisiana	Louise McFarland, DrPH	Henry B. Bradford, Jr, PhD
Maine	Kathleen F. Gensheimer, MD, MPH	Philip W. Haines, DrPH
Maryland	Diane M. Dwyer, MD, MPH	J. Mehsen Joseph, PhD
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Minnesota	Michael T. Osterholm, PhD, MPH	Pauline Bouchard, JD, MPH
Mississippi	Mary Currier, MD, MPH	Joe O. Graves, PhD
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Montana	Todd A. Damrow, PhD, MPH	Douglas O. Abbott, PhD
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North Dakota	Larry A. Shireley, MS, MPH	James D. Anders, MPH
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