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Epidemiologic Notes and Reports

Severe Isoniazid-Associated Hepatitis — New York, 1991–1993

In November 1992, the New York State Department of Health was notified of a patient who underwent liver transplantation because of severe hepatitis that developed during the use of isoniazid (INH) preventive therapy (IPT) for latent tuberculous infection. Inquiry at liver transplant centers in New York revealed other patients who had hepatitis attributed to INH. This report summarizes findings of the ongoing investigation into the extent and causes of this problem.

Transplant coordinators at the three liver transplant centers in New York and at one in Pennsylvania provided information about any patient from New York evaluated from January 1991 through May 1993 for liver transplantation because of severe acute hepatitis attributed to INH. Patients, relatives, and health-care providers were interviewed; medical records were reviewed; and histologic specimens were reexamined.

Of the 10 patients evaluated at these centers, one received both INH and rifampin. Another who had received INH had discontinued its use 1 month before onset of hepatitis symptoms because the patient had been exposed to tuberculosis (TB) resistant to INH and rifampin. Eight patients were taking INH alone (as therapy to prevent TB) at onset of hepatitis. The eight were aged 5–68 years (median: 33 years); three (38%) were aged <20 years. Six (75%) were female. Because of the severity of illness, five of the eight patients received a liver transplant. One of these patients died after transplantation. Three other patients died while awaiting a donor liver.

Circumstances leading to use of IPT were determined for seven of the eight patients; in each instance, IPT was used in accordance with current recommendations (*1*). For each, 300 mg of INH daily had been prescribed. At the time INH was prescribed, three patients were given appointments for return visits within 1 month, a practice also consistent with current recommendations; two patients were scheduled to return more than 1 month after beginning INH. Information about return visits was unavailable for three patients.

The duration of INH use before onset of hepatitis symptoms was either known or could be estimated for seven patients and ranged from 21 to 142 days (median: 57 days). For all patients, the known or estimated duration of INH use after onset of

Isoniazid-Associated Hepatitis — Continued

symptoms ranged from 3 to 49 days (median: 13 days); seven continued to take INH at least 10 days after onset of symptoms. Initial symptoms of hepatitis were fatigue in five patients, nausea in five, abdominal pain in five, and anorexia in four. All patients had jaundice when they sought medical attention.

All eight patients denied daily or intermittent heavy alcohol use. However, while taking INH, three patients took other medications associated with drug-induced hepatitis; one patient took phenytoin and estropipate; one, prednisone, methimazole, and nadolol; and one, metoclopramide. One of these patients and two other patients took acetaminophen concurrently with INH, but no patient reported using more than the recommended dosage for more than 2–3 days.

None of the patients had serologic evidence of active or chronic hepatitis B infection or of acute hepatitis A. However, two had serologic evidence of previous hepatitis B infection and two of previous hepatitis A infection. One patient had intermediate hepatitis C-antibody results that were locally interpreted as indeterminate, and five patients had negative results for hepatitis C; the other two were not tested.

Eight histologic preparations from five patients were reexamined. Six showed massive or submassive hepatic necrosis, the common finding for INH-associated hepatitis. Cholestasis was predominant for the remaining two.

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Editorial Note: INH was introduced in 1952 for treatment of TB. Its use was later expanded to include prevention of tuberculous infection (primary prophylaxis) and treatment of latent infection to prevent active TB (*2*). IPT treatment has an efficacy of up to 93% for persons with tuberculous infection who complete treatment (*3,4*).

Previous reports have described cases of severe or fatal INH-associated hepatitis (*5,6*). In one study, the estimated risk for hepatitis among persons receiving INH was 20.7 per 1000 persons; among persons with hepatitis, 4.6% of cases were fatal (*7*). In that study, the risk for hepatitis was approximately three times greater among persons aged ≥35 years than among those aged <35 years (*7*). Although 69% of persons with fatal INH-associated hepatitis have been female (*8,9*), absolute and relative risks for fatal INH-associated hepatitis cannot be determined because demographic characteristics of the total population receiving INH are unknown.

The patients described in this report had severe hepatitis that resulted in death or prompted liver transplantation. However, neither the number of persons in New York who receive IPT each year nor the number who have INH-associated hepatitis are known. Therefore, it is unclear whether the number of patients in this report represents an increase in severe or life-threatening INH-associated hepatitis (reflecting, for example, increased use of IPT) or an improvement in the detection of this problem. As in previous reports, most patients with life-threatening INH-associated hepatitis continued to take INH after the onset of symptoms.

Hepatitis in the patients described in this and previous reports appears to be temporally related to the use of INH. However, because there are no specific diagnostic criteria or pathologic findings for this problem, INH-associated hepatitis remains a

Isoniazid-Associated Hepatitis — Continued

diagnosis of exclusion. Patients who have onset of hepatitis during or after the use of INH should be evaluated for infectious, autoimmune, and toxic causes of hepatitis.

Although severe hepatitis and death may be associated with use of INH, IPT is a principal means for preventing TB and associated complications. To minimize possible risks, health-care providers should adhere to published guidelines (*1*) for selecting candidates for IPT, and patients who receive INH should be carefully monitored for adverse effects. Patients should be informed about symptoms of hepatitis and instructed to discontinue use of INH immediately if symptoms occur and to contact their health-care provider. Monthly clinical evaluation of patients taking INH is recommended, and education of patients regarding signs and symptoms of hepatitis should be continually reinforced. Health-care providers should maintain a high index of suspicion for the possibility of adverse effects and promptly report severe or fatal hepatitis associated with IPT to local or state health departments.

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Current Trends

Update: Acquired Immunodeficiency Syndrome — United States, 1992

During 1992, state and territorial health departments reported 47,095 cases of acquired immunodeficiency syndrome (AIDS) to CDC, an increase of 3.5% over the 45,499 cases reported in 1991. As in previous years, most (50.8%) cases were attributable to transmission of human immunodeficiency virus (HIV) among homosexual/bisexual men (Table 1). This report summarizes the characteristics of persons reported with AIDS in 1992, compares them with data from 1991 (Table 1), and describes selected trends since 1988.*

*Single copies of this report will be available free until July 23, 1994, from the CDCNational AIDS Clearinghouse, P.O. Box 6003, Rockville, MD 20849-6003; telephone (800) 458-5231.

AIDS — Continued

TABLE 1. Characteristics of reported persons with AIDS and percentage change in the number of cases, by year of report — United States, 1991–1992

Characteristic	1992 Reported cases No.	(%)	Rate*	1991 Reported cases	% Change 1991–1992
Sex					
Male	40,453	(85.9)	32.6	39,450	2.5
Female	6,642	(14.1)	5.1	6,049	9.8
Age (yrs)					
0– 4	624	(1.3)	3.2	535	16.6
5–12	146	(0.3)	0.5	157	–7.0
13–19	159	(0.3)	0.6	159	0
20–29	7,982	(16.9)	19.5	8,094	–1.4
30–39	21,212	(45.0)	49.1	20,764	2.2
40–49	11,963	(25.4)	36.7	11,022	8.5
50–59	3,515	(7.5)	16.0	3,357	4.7
≥60	1,494	(3.2)	3.5	1,411	5.9
Race/Ethnicity†					
White, non-Hispanic	22,328	(47.4)	11.8	22,197	0.6
Black, non-Hispanic	15,890	(33.8)	53.7	14,610	8.8
Hispanic	8,282	(17.6)	31.0	8,197	1.0
Asian/Pacific Islander	314	(0.7)	4.3	282	11.3
American Indian/ Alaskan Native	113	(0.2)	6.1	82	37.8§
Region¶					
Northeast	13,507	(28.7)	26.5	13,418	0.7
Midwest	5,296	(11.2)	8.9	4,492	17.9
South	15,788	(33.5)	18.3	15,743	0.3
West	10,881	(23.1)	20.2	10,048	8.3
U.S. territories	1,623	(3.5)	45.6	1,798	–9.7
HIV-exposure category					
Male homosexual/ bisexual contact	23,933	(50.8)	—	24,209	–1.1
History of injecting-drug use					
Women and heterosexual men	11,423	(24.3)	—	11,313	1.0
Male homosexual/ bisexual contact	2,429	(5.2)	—	2,549	–4.7
Persons with hemophilia					
Adult/Adolescent	316	(0.7)	—	316	0
Child (aged <13 yrs)	21	(<0.1)	—	25	–16.0§
Transfusion recipients					
Adult/Adolescent	673	(1.4)	—	695	–3.2
Child (aged <13 yrs)	19	(<0.1)	—	39	–51.3§
Heterosexual contacts**	4,111	(8.7)	—	3,510	17.1
Perinatal	696	(1.5)	—	614	13.4
No identified risk	3,474	(7.3)	—	2,229	—
Total	**47,095**	**(100.0)**	**18.5**	**45,499**	**3.5**

* Per 100,000 population. 1992 population counts were estimated from 1990 U.S. Census Bureau data. For categories of sex, age, race/ethnicity, and HIV exposure, denominator was population in 50 states and Puerto Rico (excluding other U.S. territories).

†Excludes persons with unspecified race/ethnicity (168 [0.4%] in 1992, 131 [0.3%] in 1991).

§Estimate of percentage change in cases may be less reliable because of small number of cases.

¶Northeast=New England and Middle Atlantic regions; Midwest=East North Central and West North Central regions; South=South Atlantic, East South Central, and West South Central regions; West=Mountain and Pacific regions.

** Includes persons born in countries where heterosexual transmission is believed to be the predominant mode of transmission.

AIDS — Continued

From 1991 through 1992, larger proportionate increases in reported cases occurred among women (9.8%) than among men (2.5%). For women, rates were higher for non-Hispanic blacks and Hispanics (31.3 and 14.6 per 100,000 population, respectively) than for non-Hispanic whites (1.8). Ten metropolitan statistical areas† accounted for more than half (51.5%) of reported cases among women (Table 2).

The number of reported cases among homosexual/bisexual men decreased during 1992, sustaining a trend noted first in 1991 (*1*); the number of cases attributable to injecting-drug use (IDU) increased slightly, representing nearly one fourth of reported cases. Heterosexual contact accounted for the largest proportionate increase (17.1%) in reported cases. The proportionate increase in cases attributed to heterosexual contact was greater for men (26.3%) than for women (11.5%); however, women accounted for most persons infected through heterosexual contact (59.4%). The second largest proportionate increase was in perinatal transmission (13.4%).

Because cases reported in a year may have been diagnosed in earlier years, long-term trends in the occurrence of AIDS are reflected more accurately by analyses based on year of diagnosis with adjustment for reporting delays (*2*). From 1988 through 1991, the number of cases diagnosed among women infected through IDU exceeded those among women infected through heterosexual contact. However, in 1992, the number of AIDS cases among women infected through heterosexual contact exceeded those infected through IDU for the first time (Figure 1). This pattern varied by region: IDU was the predominant mode of transmission among women in the Northeast§; however, heterosexual transmission equaled or surpassed IDU among women

†Metropolitan statistical areas typically include the main city as well as the surrounding urban and suburban areas.
§New England and Middle Atlantic regions.

TABLE 2. Rate* of AIDS among women in 10 metropolitan statistical areas† reporting the highest numbers of AIDS cases among women, by race/ethnicity§ — United States, 1992

City	No.	Rate			
		White, non-Hispanic	Black, non-Hispanic	Hispanic	Overall
New York City	1581	10.2	90.9	71.7	**41.5**
West Palm Beach, Fla.	147	7.5	295.4	24.3	**38.1**
Ft. Lauderdale, Fla.	191	8.0	199.5	22.6	**34.1**
Newark, N.J.	235	4.6	105.5	31.3	**29.6**
Miami	244	7.7	125.2	9.5	**29.1**
San Juan, P.R.	201	0	0	26.8	**26.8**
Baltimore	190	2.8	64.2	17.5	**18.6**
Washington, D.C.	171	1.6	33.3	4.6	**10.2**
Chicago	210	2.8	23.4	12.1	**8.2**
Los Angeles	163	2.1	14.3	5.6	**4.5**

*Per 100,000 women.
†Metropolitan statistical areas typically include the main city as well as the surrounding urban and suburban areas.
§Numbers for other racial/ethnic groups were too small for meaningful analysis.

AIDS — Continued

in the South¶, the Midwest**, the West††, and the U.S. territories. Among those cases attributed to heterosexual transmission, most (56.8%) involved sex with an injecting-drug user.

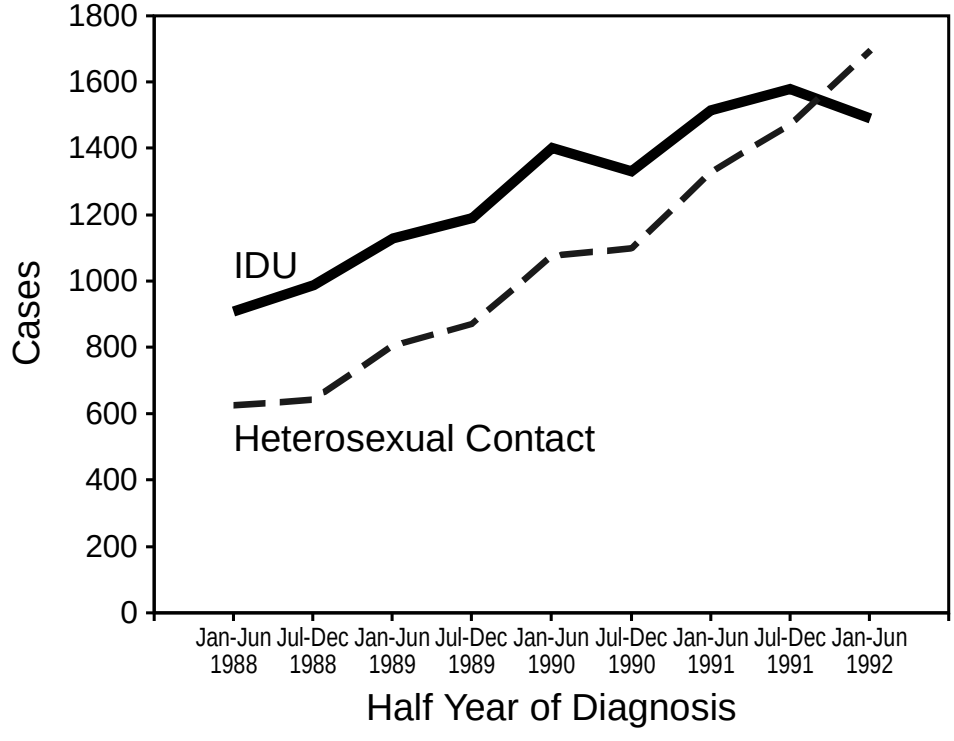
Heterosexual transmission accounted for a greater proportion of AIDS cases among women aged 20–29 years than among women aged ≥30 years (60.0% and 46.5%, respectively). The annual number of cases diagnosed among all persons aged 20–29 years increased by 15.5% since 1988; however, the annual number of women aged 20–29 years with heterosexually acquired AIDS increased by 96.7% since 1988. This trend primarily reflects a larger increase among non-Hispanic black women than among non-Hispanic whites and Hispanic women (Figure 2). In addition, the greatest increase among women aged 20–29 years with heterosexually acquired AIDS was in the South (165.5% since 1988).

Reported by: Local, state, and territorial health depts. Div of HIV/AIDS, National Center for Infectious Diseases, CDC.

Editorial Note: The findings in this report reflect the evolving nature of the HIV epidemic in the United States, which is a composite of multiple epidemics in different regions and among different population subgroups. During 1992, the rate of increase in AIDS cases was again higher for women than for men, and heterosexual contact

¶South Atlantic, East South Central, and West South Central regions.
**East North Central and West North Central regions.
††Mountain and Pacific regions.

FIGURE 1. AIDS cases among women attributed to injecting-drug use (IDU) and heterosexual contact, by half year of diagnosis* — United States, 1988–1992



*Adjusted for reporting delays.

AIDS — Continued

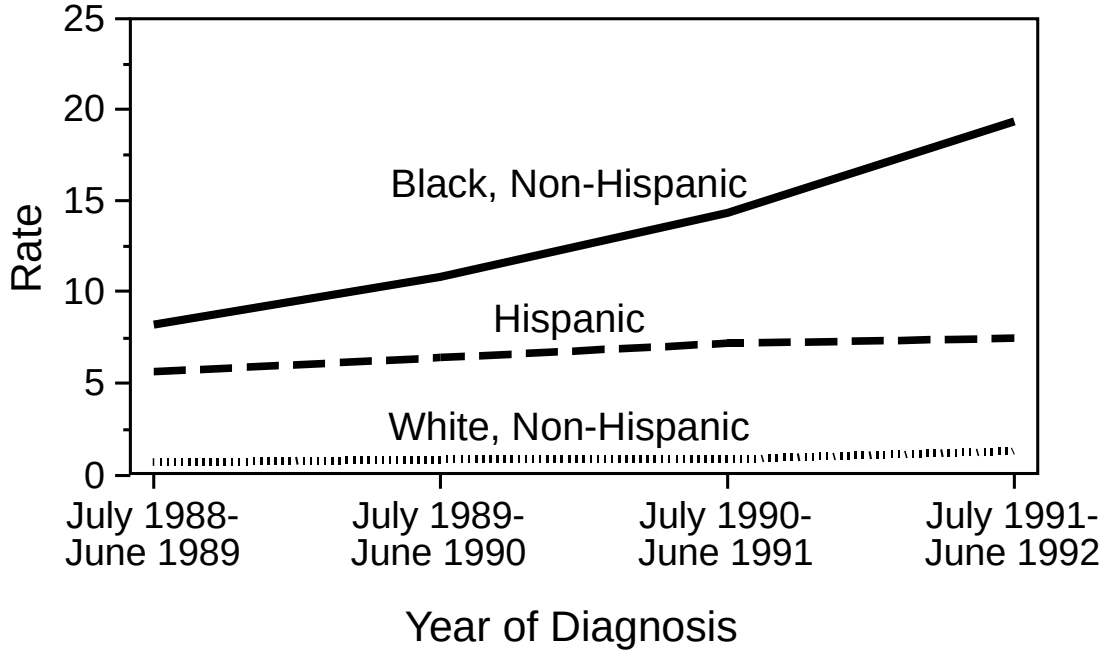
became the predominant mode of HIV exposure among women in whom AIDS was diagnosed; most heterosexual transmission occurred among women who were sex partners of injecting-drug users. The increase in AIDS among women is reflected by an increase in cases among infants and children aged 0–4 years, most (95.8%) of whom were infected perinatally.

The increase in cases among women aged 20–29 years primarily reflects persons who were infected as adolescents. Many adolescents, like adults, practice behaviors that increase their risk for HIV infection (*3*). However, even though adolescents have adequate levels of knowledge about AIDS (*4*), they may be particularly resistant to behavior change because of feelings of invulnerability that are characteristic of adolescence. Developing and implementing educational programs specific to adolescents should remain a high priority.

Because race and ethnicity are likely risk markers and not risk factors for HIV infection, these markers may assist in identifying groups at highest risk for HIV infection and targeting prevention efforts. The higher incidence of AIDS among non-Hispanic blacks and Hispanics than among non-Hispanic whites probably reflects a combination of such risk factors, including socioeconomic status and access to medical care.

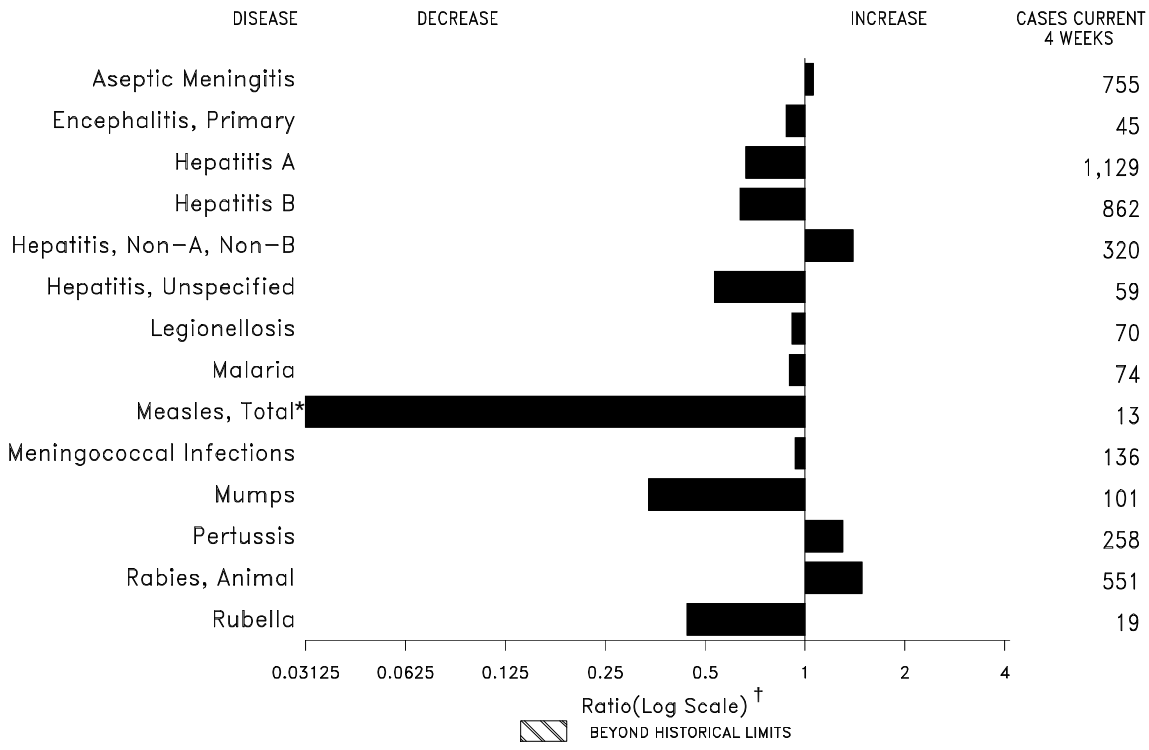
(Continued on page 557)

FIGURE 2. Rate* of heterosexually acquired AIDS among 20–29-year-old women, by race/ethnicity† and year of diagnosis§ — United States, 1988–1992



*Per 100,000 women.
†Numbers for other racial/ethnic groups were too small for meaningful analysis.
§Adjusted for reporting delays.

FIGURE I. Notifiable disease reports, comparison of 4-week totals ending July 17, 1993, with historical data — United States



*The large apparent decrease in reported cases of measles(total) reflects dramatic fluctuations in the historical baseline. (Ratio (log scale) for week twenty-eight is 0.01581).

† Ratio of current 4-week total to mean of 15 4-week totals (from previous, comparable, and subsequent 4-week periods for the past 5 years). The point where thehatched area begins is based on the mean and two standard deviations of these 4-week totals.

TABLE I. Summary — cases of specified notifiable diseases, United States, cumulative, week ending July 17, 1993 (28th Week)

	Cum. 1993		Cum. 1993
AIDS*	59,979	Measles: imported	18
Anthrax	-	indigenous	159
Botulism: Foodborne	8	Plague	3
Infant	15	Poliomyelitis, Paralytic§	-
Other	2	Psittacosis	28
Brucellosis	47	Rabies, human	-
Cholera	14	Syphilis, primary & secondary	14,117
Congenital rubella syndrome	5	Syphilis, congenital, age < 1 year¶	677
Diphtheria	-	Tetanus	15
Encephalitis, post-infectious	91	Toxic shock syndrome	128
Gonorrhea	205,026	Trichinosis	8
Haemophilus influenzae (invasive disease)†	684	Tuberculosis	10,944
Hansen Disease	92	Tularemia	60
Leptospirosis	19	Typhoid fever	172
Lyme Disease	2,641	Typhus fever, tickborne (RMSF)	133

*Updated monthly; last update July 3, 1993.
†Of 626 cases of known age, 207 (33%) were reported among children less than 5 years of age.
§No cases of suspected poliomyelitis have been reported in 1993; 10 cases of suspected poliomyelitis were reported in 1992; 6 of the 9 suspected cases with onset in 1991 were confirmed; the confirmed cases were vaccine associated.
¶Reports through first quarter 1993.

TABLE II. Cases of selected notifiable diseases, United States, weeks ending July 17, 1993, and July 11, 1992 (28th Week)

Reporting Area	AIDS*	Aseptic Meningitis	Encephalitis		Gonorrhea		Hepatitis (Viral), by type				Legionellosis	Lyme Disease
			Primary	Post-infectious			A	B	NA,NB	Unspecified		
	Cum. 1993	Cum. 1993	Cum. 1993	Cum. 1993	Cum. 1993	Cum. 1992	Cum. 1993	Cum. 1993	Cum. 1993	Cum. 1993	Cum. 1993	Cum. 1993
UNITED STATES	59,979	3,972	288	91	205,026	262,293	11,239	6,440	2,452	336	588	2,641
NEW ENGLAND	2,815	61	5	4	4,055	5,444	160	188	250	5	15	529
Maine	60	12	1	-	46	49	8	9	-	-	4	4
N.H.	66	12	-	2	37	68	13	50	228	1	1	26
Vt.	14	11	3	-	14	14	3	5	2	-	-	3
Mass.	1,491	11	1	2	1,309	1,999	47	73	16	4	6	24
R.I.	192	15	-	-	197	405	49	15	4	-	4	85
Conn.	992	-	-	-	2,452	2,909	40	36	-	-	-	387
MID. ATLANTIC	13,675	337	14	7	23,130	27,802	634	803	178	4	121	1,626
Upstate N.Y.	2,162	142	7	4	4,386	5,675	211	222	107	1	37	1,076
N.Y. City	7,455	104	1	-	6,056	9,357	177	121	1	-	3	3
N.J.	2,561	-	-	-	3,853	4,044	167	230	49	-	16	234
Pa.	1,497	91	6	3	8,835	8,726	79	230	21	3	65	313
E.N. CENTRAL	4,967	506	81	17	39,882	48,578	1,284	788	369	8	159	20
Ohio	809	163	27	3	11,255	14,755	167	124	29	-	77	15
Ind.	585	71	6	7	4,031	4,441	434	129	7	1	34	1
Ill.	1,776	102	18	2	12,862	15,859	310	129	21	2	8	2
Mich.	1,290	160	26	5	8,832	11,267	123	238	291	5	32	2
Wis.	507	10	4	-	2,902	2,256	250	168	21	-	8	-
W.N. CENTRAL	2,274	243	14	-	10,787	13,871	1,394	350	88	10	40	59
Minn.	480	48	6	-	1,355	1,620	246	35	3	4	1	21
Iowa	131	47	1	-	602	930	19	13	5	1	5	5
Mo.	1,292	52	-	-	6,226	7,596	883	253	61	5	11	7
N. Dak.	-	8	3	-	25	52	53	-	-	-	1	2
S. Dak.	21	7	3	-	158	92	11	-	-	-	-	-
Nebr.	120	5	-	-	476	896	123	10	9	-	19	3
Kans.	230	76	1	-	1,945	2,685	59	39	10	-	3	21
S. ATLANTIC	12,950	966	53	38	54,905	81,442	702	1,215	314	42	107	320
Del.	235	22	3	-	743	935	7	81	66	-	8	141
Md.	1,425	90	13	-	8,729	7,769	96	155	8	5	23	49
D.C.	774	20	-	-	2,885	3,723	5	28	-	-	12	2
Va.	899	97	17	3	6,148	9,547	87	81	20	15	3	32
W. Va.	46	8	9	-	317	484	4	21	16	-	1	2
N.C.	742	70	10	-	13,531	13,567	37	172	33	-	15	53
S.C.	854	7	-	-	5,498	5,962	8	23	-	1	11	4
Ga.	1,661	62	1	-	4,660	25,287	63	99	41	-	22	16
Fla.	6,314	590	-	35	12,394	14,168	395	555	130	21	12	21
E.S. CENTRAL	1,588	230	12	5	23,500	25,285	137	654	482	1	23	11
Ky.	185	88	6	4	2,440	2,605	69	49	8	-	8	2
Tenn.	640	34	5	-	6,892	8,181	28	540	465	-	11	7
Ala.	490	69	1	-	8,740	8,382	28	62	4	1	2	2
Miss.	273	39	-	1	5,428	6,117	12	3	5	-	2	-
W.S. CENTRAL	6,332	410	22	-	24,199	28,342	1,040	845	134	102	15	14
Ark.	248	23	-	-	4,631	4,385	26	32	2	1	-	1
La.	806	36	1	-	6,446	8,101	46	109	51	2	2	-
Okla.	542	1	4	-	1,931	2,831	65	141	42	6	9	6
Tex.	4,736	350	17	-	11,191	13,025	903	563	39	93	4	7
MOUNTAIN	2,789	229	14	4	5,817	6,642	2,252	317	168	55	49	4
Mont.	17	-	-	1	31	57	55	4	-	-	5	-
Idaho	49	7	-	-	98	63	98	26	-	1	1	-
Wyo.	30	4	-	-	48	29	11	16	53	-	5	2
Colo.	925	47	4	-	1,777	2,410	553	41	27	35	5	-
N. Mex.	220	47	3	2	496	492	188	125	53	2	3	-
Ariz.	956	87	5	-	2,192	2,279	800	52	10	7	9	-
Utah	195	6	1	-	183	157	490	25	19	10	7	1
Nev.	397	31	1	1	992	1,155	57	28	6	-	14	1
PACIFIC	12,589	990	73	16	18,751	24,887	3,636	1,280	469	109	59	58
Wash.	882	-	-	-	2,046	2,232	405	112	100	7	9	1
Oreg.	522	-	-	-	984	868	55	21	9	-	-	1
Calif.	11,030	923	69	16	15,138	21,136	2,677	1,125	350	99	45	55
Alaska	20	9	3	-	263	387	448	6	8	-	-	-
Hawaii	135	58	1	-	320	264	51	16	2	3	5	1
Guam	-	2	-	-	38	45	2	2	-	1	-	-
P.R.	1,786	31	-	-	259	98	45	222	25	2	-	-
V.I.	33	-	-	-	63	57	-	2	-	-	-	-
Amer. Samoa	-	-	-	-	30	21	12	-	-	-	-	-
C.N.M.I.	-	2	-	-	47	41	-	-	-	1	-	-

N: Not notifiable U: Unavailable C.N.M.I.: Commonwealth of Northern Mariana Islands

*Updated monthly; last update July 3, 1993.

TABLE II. (Cont'd.) Cases of selected notifiable diseases, United States, weeks ending July 17, 1993, and July 11, 1992 (28th Week)

Reporting Area	Malaria	Measles (Rubeola)					Menin-gococcal Infections	Mumps		Pertussis			Rubella		
		Indigenous		Imported*		Total									
	Cum. 1993	1993	Cum. 1993	1993	Cum. 1993	Cum. 1992	Cum. 1993	1993	Cum. 1993	1993	Cum. 1993	Cum. 1992	1993	Cum. 1993	Cum. 1992
UNITED STATES	515	-	159	-	18	2,023	1,414	23	974	86	1,565	956	5	126	114
NEW ENGLAND	24	-	42	-	3	51	59	1	6	15	328	82	-	1	6
Maine	1	-	-	-	-	-	5	-	-	-	8	3	-	1	1
N.H.	5	-	-	-	-	13	12	-	-	4	202	26	-	-	-
Vt.	1	-	30	-	1	-	4	-	-	1	45	2	-	-	-
Mass.	2	-	3	-	1	14	18	-	-	9	35	36	-	-	-
R.I.	2	-	-	-	1	20	1	-	2	-	3	-	-	-	4
Conn.	13	-	9	-	-	4	19	1	4	1	35	15	-	-	1
MID. ATLANTIC	92	-	6	-	2	193	178	2	78	13	211	53	-	35	10
Upstate N.Y.	32	-	-	-	1	109	81	1	27	4	89	25	-	10	7
N.Y. City	24	-	2	-	-	48	19	-	-	-	7	9	-	15	-
N.J.	26	-	4	-	1	36	25	-	8	-	21	19	-	6	3
Pa.	10	-	-	-	-	-	53	1	43	9	94	-	-	4	-
E.N. CENTRAL	29	-	1	-	-	39	215	1	140	9	263	99	-	2	7
Ohio	7	-	-	-	-	5	63	-	57	8	128	26	-	1	-
Ind.	3	U	-	U	-	20	33	U	3	U	29	14	U	-	-
Ill.	14	-	1	-	-	8	59	-	29	-	20	17	-	-	7
Mich.	5	-	-	-	-	4	41	1	48	1	20	4	-	-	-
Wis.	-	-	-	-	-	2	19	-	3	-	66	38	-	1	-
W.N. CENTRAL	16	-	1	-	2	10	89	1	28	6	105	80	-	1	5
Minn.	3	-	-	-	-	9	6	1	1	5	51	25	-	-	-
Iowa	1	-	-	-	-	1	16	-	7	-	1	3	-	-	-
Mo.	4	-	1	-	-	-	33	-	15	-	30	32	-	1	1
N. Dak.	2	-	-	-	-	-	3	-	4	-	3	8	-	-	-
S. Dak.	2	-	-	-	-	-	3	-	-	-	2	5	-	-	-
Nebr.	3	-	-	-	-	-	7	-	1	1	7	3	-	-	-
Kans.	1	-	-	-	2	-	21	-	-	-	11	4	-	-	4
S. ATLANTIC	157	-	20	-	3	114	284	4	307	21	173	66	-	8	11
Del.	2	-	3	-	-	1	11	-	4	-	5	1	-	2	-
Md.	15	-	-	-	2	16	30	-	54	14	64	13	-	2	4
D.C.	5	-	-	-	-	-	5	-	-	-	2	-	-	-	-
Va.	12	-	-	-	1	11	25	-	16	-	17	4	-	-	-
W. Va.	2	-	-	-	-	-	11	2	8	2	8	2	-	-	-
N.C.	83	-	-	-	-	24	53	-	176	-	24	14	-	-	-
S.C.	1	-	-	-	-	29	24	-	14	-	5	7	-	-	2
Ga.	8	-	-	-	-	-	59	1	10	-	5	8	-	-	-
Fla.	29	-	17	-	-	33	66	1	25	5	43	17	-	4	5
E.S. CENTRAL	14	-	1	-	-	454	87	1	35	2	66	16	-	-	1
Ky.	-	-	-	-	-	437	17	-	-	-	3	-	-	-	-
Tenn.	7	-	-	-	-	-	19	-	11	1	34	5	-	-	1
Ala.	3	-	1	-	-	-	32	1	19	1	27	10	-	-	-
Miss.	4	-	-	-	-	17	19	-	5	-	2	1	-	-	-
W.S. CENTRAL	13	-	1	-	-	1,049	128	5	143	8	44	133	4	16	6
Ark.	2	-	-	-	-	-	14	-	4	-	3	6	-	-	-
La.	-	-	1	-	-	-	25	1	12	-	6	-	-	1	-
Okla.	4	-	-	-	-	11	15	1	8	8	22	21	-	1	-
Tex.	7	-	-	-	-	1,038	74	3	119	-	13	106	4	14	6
MOUNTAIN	17	-	2	-	-	15	121	1	36	8	129	152	-	4	5
Mont.	2	-	-	-	-	-	11	-	-	1	1	1	-	-	-
Idaho	1	-	-	-	-	-	7	-	5	7	28	17	-	1	1
Wyo.	-	-	-	-	-	1	2	-	2	-	1	-	-	-	-
Colo.	10	-	2	-	-	14	20	-	8	-	50	25	-	-	-
N. Mex.	4	-	-	-	-	-	3	N	N	-	21	32	-	-	-
Ariz.	-	-	-	-	-	-	61	-	6	-	12	61	-	1	2
Utah	-	-	-	-	-	-	10	-	3	-	16	15	-	1	1
Nev.	-	-	-	-	-	-	7	1	12	-	-	1	-	1	1
PACIFIC	153	-	85	-	8	98	253	7	201	4	246	275	1	59	63
Wash.	16	-	-	-	-	10	41	-	8	-	22	69	-	-	6
Oreg.	3	-	-	-	-	3	21	N	N	-	3	14	-	1	1
Calif.	130	-	74	-	3	48	171	6	172	4	211	171	-	34	36
Alaska	-	-	-	-	-	9	12	-	5	-	3	4	-	1	-
Hawaii	4	-	11	-	5	28	8	1	16	-	7	17	1	23	20
Guam	1	U	2	U	-	10	1	U	6	U	-	-	U	-	1
P.R.	-	-	159	-	-	253	6	-	1	-	1	9	-	-	-
V.I.	-	-	-	-	-	-	-	-	3	-	-	-	-	-	-
Amer. Samoa	-	-	1	-	-	-	-	-	-	-	2	6	-	-	-
C.N.M.I.	-	U	-	U	1	-	-	U	11	U	-	1	U	-	-

*For measles only, imported cases include both out-of-state and international importations.
N: Not notifiable U: Unavailable † International § Out-of-state

TABLE II. (Cont'd.) Cases of selected notifiable diseases, United States, weeks ending July 17, 1993, and July 11, 1992 (28th Week)

Reporting Area	Syphilis (Primary & Secondary)		Toxic-Shock Syndrome	Tuberculosis		Tula-remia	Typhoid Fever	Typhus Fever (Tick-borne) (RMSF)	Rabies, Animal
	Cum. 1993	Cum. 1992	Cum. 1993	Cum. 1993	Cum. 1992	Cum. 1993	Cum. 1993	Cum. 1993	Cum. 1993
UNITED STATES	14,117	18,392	128	10,944	11,438	60	172	133	4,277
NEW ENGLAND	231	345	7	227	177	-	12	2	559
Maine	3	2	2	7	14	-	-	-	-
N.H.	25	26	2	4	-	-	1	-	40
Vt.	1	1	-	3	3	-	-	-	18
Mass.	86	166	2	125	74	-	7	2	92
R.I.	9	19	1	32	13	-	-	-	-
Conn.	107	131	-	56	73	-	4	-	409
MID. ATLANTIC	1,343	2,600	25	2,428	2,784	1	46	12	1,744
Upstate N.Y.	117	206	14	221	342	1	11	1	1,264
N.Y. City	681	1,432	1	1,451	1,626	-	26	-	-
N.J.	183	357	-	394	472	-	6	7	304
Pa.	362	605	10	362	344	-	3	4	176
E.N. CENTRAL	2,178	2,706	36	1,129	1,152	3	16	6	38
Ohio	649	404	15	171	174	1	5	5	4
Ind.	179	131	1	120	92	1	1	-	-
Ill.	796	1,204	5	551	570	-	5	1	5
Mich.	340	546	15	238	269	1	4	-	3
Wis.	214	421	-	49	47	-	1	-	26
W.N. CENTRAL	913	723	9	242	260	19	2	9	202
Minn.	49	46	2	30	75	-	-	1	27
Iowa	32	28	5	30	23	-	-	1	35
Mo.	736	548	-	125	105	8	2	5	5
N. Dak.	-	1	-	4	3	-	-	-	42
S. Dak.	1	-	-	10	14	8	-	2	25
Nebr.	10	19	-	12	13	1	-	-	6
Kans.	85	81	2	31	27	2	-	-	62
S. ATLANTIC	3,739	5,120	15	1,861	2,101	1	22	60	1,101
Del.	73	125	1	21	25	-	1	1	86
Md.	213	381	-	206	151	-	3	5	322
D.C.	207	236	-	88	69	-	-	-	9
Va.	337	417	3	237	157	-	2	4	200
W. Va.	5	9	-	44	40	-	-	1	47
N.C.	1,053	1,287	3	270	271	-	-	27	45
S.C.	566	679	-	232	217	-	-	6	91
Ga.	611	1,042	2	415	465	-	1	11	259
Fla.	674	944	6	348	706	1	15	5	42
E.S. CENTRAL	2,028	2,379	5	715	836	3	2	13	52
Ky.	168	80	2	200	209	-	-	5	10
Tenn.	575	677	1	144	235	2	-	6	-
Ala.	453	918	2	251	226	1	2	-	42
Miss.	832	704	-	120	166	-	-	2	-
W.S. CENTRAL	2,995	3,169	2	1,126	1,104	26	2	27	333
Ark.	480	497	-	97	93	14	-	-	18
La.	1,342	1,363	-	-	87	-	1	1	4
Okla.	225	145	2	155	73	9	-	25	49
Tex.	948	1,164	-	874	851	3	1	1	262
MOUNTAIN	130	212	8	251	303	3	5	4	63
Mont.	1	6	-	5	-	-	-	-	12
Idaho	-	1	1	6	12	-	-	-	2
Wyo.	4	1	-	2	-	2	-	4	11
Colo.	35	31	2	8	30	-	4	-	1
N. Mex.	19	24	-	35	47	-	-	-	4
Ariz.	56	102	1	126	129	-	1	-	29
Utah	3	6	3	11	42	1	-	-	-
Nev.	12	41	1	58	43	-	-	-	4
PACIFIC	560	1,138	21	2,965	2,721	4	65	-	185
Wash.	28	53	4	133	165	1	4	-	-
Oreg.	48	25	-	57	63	2	-	-	-
Calif.	478	1,052	17	2,608	2,323	1	59	-	168
Alaska	4	3	-	27	38	-	-	-	17
Hawaii	2	5	-	140	132	-	2	-	-
Guam	1	2	-	28	34	-	-	-	-
P.R.	302	170	-	113	135	-	-	-	26
V.I.	31	35	-	2	3	-	-	-	-
Amer. Samoa	-	-	-	2	-	-	-	-	-
C.N.M.I.	3	4	-	19	37	-	-	-	-

U: Unavailable

TABLE III. Deaths in 121 U.S. cities,* week ending July 17, 1993 (28th Week)

Reporting Area	All Causes, By Age (Years)						P&I† Total
	All Ages	≥65	45-64	25-44	1-24	<1	
NEW ENGLAND	605	435	101	41	12	16	49
Boston, Mass.	156	101	30	13	3	9	20
Bridgeport, Conn.	45	34	4	6	1	-	4
Cambridge, Mass.	22	16	4	2	-	-	3
Fall River, Mass.	43	33	7	3	-	-	1
Hartford, Conn.	56	38	12	4	1	1	-
Lowell, Mass.	27	20	6	1	-	-	-
Lynn, Mass.	12	11	1	-	-	-	1
New Bedford, Mass.	32	22	7	1	2	-	1
New Haven, Conn.	54	37	8	4	2	3	5
Providence, R.I.	40	30	7	1	2	-	-
Somerville, Mass.	5	5	-	-	-	-	-
Springfield, Mass.	34	25	4	2	1	2	4
Waterbury, Conn.	25	21	3	1	-	-	5
Worcester, Mass.	54	42	8	3	-	1	5
MID. ATLANTIC	2,502	1,575	496	311	72	48	94
Albany, N.Y.	55	38	11	3	1	2	-
Allentown, Pa.	23	19	1	3	-	-	-
Buffalo, N.Y.	101	76	15	5	4	1	3
Camden, N.J.	59	36	11	6	3	3	3
Elizabeth, N.J.	42	29	10	3	-	-	3
Erie, Pa.§	40	25	10	3	1	1	1
Jersey City, N.J.	56	33	8	14	-	1	5
New York City, N.Y.	1,464	920	279	202	39	24	50
Newark, N.J.	86	34	25	18	5	4	2
Paterson, N.J.	23	11	7	4	-	1	-
Philadelphia, Pa.	200	119	46	23	8	4	6
Pittsburgh, Pa.§	51	32	14	4	-	1	5
Reading, Pa.	11	10	-	-	1	-	-
Rochester, N.Y.	132	92	21	7	8	4	10
Schenectady, N.Y.	17	12	3	2	-	-	-
Scranton, Pa.§	35	19	13	1	-	2	-
Syracuse, N.Y.	49	32	12	5	-	-	1
Trenton, N.J.	37	23	7	7	-	-	4
Utica, N.Y.	21	15	3	1	2	-	1
Yonkers, N.Y.	U	U	U	U	U	U	U
E.N. CENTRAL	2,050	1,330	366	196	100	58	106
Akron, Ohio	69	50	12	1	1	5	-
Canton, Ohio	28	23	5	-	-	-	4
Chicago, Ill.	283	125	53	48	51	6	11
Cincinnati, Ohio	115	78	27	5	4	1	9
Cleveland, Ohio	142	94	29	10	5	4	2
Columbus, Ohio	192	134	36	16	-	6	13
Dayton, Ohio	110	81	16	7	3	3	4
Detroit, Mich.	285	170	47	40	15	13	5
Evansville, Ind.	56	34	12	6	2	2	2
Fort Wayne, Ind.	49	35	8	5	1	-	2
Gary, Ind.	24	15	3	4	2	-	1
Grand Rapids, Mich.	41	26	6	3	3	3	5
Indianapolis, Ind.	192	128	37	18	4	5	16
Madison, Wis.	41	25	9	6	1	-	2
Milwaukee, Wis.	157	122	22	9	1	3	9
Peoria, Ill.	43	29	7	4	2	1	5
Rockford, Ill.	39	30	6	3	-	-	4
South Bend, Ind.	39	28	8	2	-	1	3
Toledo, Ohio	89	61	14	7	3	4	8
Youngstown, Ohio	56	42	9	2	2	1	1
W.N. CENTRAL	700	503	109	49	28	10	36
Des Moines, Iowa	U	U	U	U	U	U	U
Duluth, Minn.	36	27	6	3	-	-	-
Kansas City, Kans.	41	28	4	7	-	1	-
Kansas City, Mo.	110	83	13	6	6	2	5
Lincoln, Nebr.	50	41	5	4	-	-	6
Minneapolis, Minn.	147	106	27	7	5	2	7
Omaha, Nebr.	83	64	10	4	3	2	3
St. Louis, Mo.	100	63	18	9	7	3	6
St. Paul, Minn.	59	48	7	3	1	-	4
Wichita, Kans.	74	43	19	6	6	-	5

Reporting Area	All Causes, By Age (Years)						P&I† Total
	All Ages	≥65	45-64	25-44	1-24	<1	
S. ATLANTIC	1,226	728	240	166	52	39	45
Atlanta, Ga.	U	U	U	U	U	U	U
Baltimore, Md.	291	178	54	38	18	3	17
Charlotte, N.C.	50	26	9	10	2	3	2
Jacksonville, Fla.	123	71	32	11	3	6	2
Miami, Fla.	107	65	19	21	1	1	-
Norfolk, Va.	62	40	12	7	2	1	3
Richmond, Va.	78	42	20	8	7	-	-
Savannah, Ga.	56	40	10	5	-	1	7
St. Petersburg, Fla.	56	42	5	7	1	1	3
Tampa, Fla.	170	114	31	17	3	5	10
Washington, D.C.	221	103	46	39	15	18	1
Wilmington, Del.	12	7	2	3	-	-	-
E.S. CENTRAL	655	425	134	59	18	19	45
Birmingham, Ala.	116	77	25	9	3	2	3
Chattanooga, Tenn.	50	30	15	2	1	2	3
Knoxville, Tenn.	89	60	20	7	2	-	9
Lexington, Ky.	61	40	13	5	1	2	6
Memphis, Tenn.	155	92	28	18	7	10	9
Mobile, Ala.	28	21	4	2	1	-	4
Montgomery, Ala.	39	25	8	5	1	-	3
Nashville, Tenn.	117	80	21	11	2	3	8
W.S. CENTRAL	1,444	880	294	168	59	43	83
Austin, Tex.	69	47	10	9	3	-	10
Baton Rouge, La.	52	30	12	6	2	2	2
Corpus Christi, Tex.	36	23	10	2	1	-	3
Dallas, Tex.	196	108	36	35	11	6	3
El Paso, Tex.	61	45	9	4	1	2	4
Ft. Worth, Tex.	100	62	21	10	1	6	2
Houston, Tex.	381	210	94	52	14	11	28
Little Rock, Ark.	70	48	11	3	6	2	6
New Orleans, La.	97	58	22	12	3	2	-
San Antonio, Tex.	220	143	39	22	12	4	10
Shreveport, La.	60	34	13	4	3	6	7
Tulsa, Okla.	102	72	17	9	2	2	8
MOUNTAIN	765	502	139	79	31	14	51
Albuquerque, N.M.	87	56	15	10	4	2	2
Colo. Springs, Colo.	39	27	5	5	1	1	4
Denver, Colo.	133	76	32	16	6	3	11
Las Vegas, Nev.	107	66	23	9	3	6	3
Ogden, Utah	34	25	6	2	1	-	3
Phoenix, Ariz.	137	84	21	20	10	2	15
Pueblo, Colo.	23	19	4	-	-	-	1
Salt Lake City, Utah	83	59	14	7	3	-	4
Tucson, Ariz.	122	90	19	10	3	-	8
PACIFIC	2,145	1,405	383	219	85	51	134
Berkeley, Calif.	14	7	3	3	1	-	-
Fresno, Calif.	191	135	26	10	13	7	10
Glendale, Calif.	23	17	3	3	-	-	2
Honolulu, Hawaii	65	46	11	7	-	1	5
Long Beach, Calif.	82	61	12	3	4	2	12
Los Angeles, Calif.	558	331	123	69	29	4	15
Pasadena, Calif.	38	28	2	5	2	1	2
Portland, Oreg.	160	106	26	15	5	8	6
Sacramento, Calif.	188	119	39	16	8	6	19
San Diego, Calif.	177	118	31	14	5	9	23
San Francisco, Calif.	157	77	38	35	3	4	2
San Jose, Calif.	180	138	23	11	2	6	21
Santa Cruz, Calif.	28	20	5	3	-	-	2
Seattle, Wash.	151	101	19	19	10	2	4
Spokane, Wash.	41	31	8	1	1	-	1
Tacoma, Wash.	92	70	14	5	2	1	10
TOTAL	12,092¶	7,783	2,262	1,288	457	298	643

*Mortality data in this table are voluntarily reported from 121 cities in the United States, most of which have populations of 100,000 or more. A death is reported by the place of its occurrence and by the week that the death certificate was filed. Fetal deaths are not included.

†Pneumonia and influenza.

§Because of changes in reporting methods in these 3 Pennsylvania cities, these numbers are partial counts for the current week. Complete counts will be available in 4 to 6 weeks.

¶Total includes unknown ages.

U: Unavailable.

AIDS — Continued

Because of the hierarchical classification of risk (*5*), and because risk information may not always be complete or verified, AIDS surveillance probably approximates the actual frequency of heterosexual transmission. During 1992, 10.2% of men and 23.5% of women who reported IDU also reported heterosexual contact with a person at risk. Therefore, some of these persons may have acquired HIV through heterosexual contact. Conversely, some persons with AIDS attributed to heterosexual contact may have other unreported or undetermined risk factors (*6*).

The steady increase in heterosexually acquired AIDS cases among men and women underscores the need to improve understanding of factors that influence the adoption of safer sexual practices among heterosexuals and how these factors vary in different population subgroups. Although some surveys have documented reduced number of sex partners among high school students and persons who attend sexually transmitted diseases clinics (*7,8*), a survey of the general heterosexual population (*9*) found low rates of condom use for persons with multiple partners and for persons with partners at risk for HIV infection, indicating that behavioral changes sufficient to decrease HIV transmission may not yet have occurred.

The findings in this report indicate that the number of AIDS cases attributed to male-to-male sexual transmission has decreased slightly, and the proportionate increase in cases attributed to IDU was less than that in cases attributed to heterosexual contact. However, because injecting-drug users and men who have sex with men continue to account for 80.3% of AIDS cases, prevention efforts that target these populations must remain a high priority while interventions targeted at persons at increased risk for heterosexual transmission are strengthened.

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Epidemiologic Notes and Reports

Heat-Related Deaths — United States, 1993

From July 1 through July 13, 1993, the heat wave in the eastern United States has been implicated as the direct cause of or a contributing factor to 84 deaths among persons residing in the Philadelphia area. In Philadelphia County, the medical examiner (ME) lists hyperthermia as a contributing factor leading to death if a decedent is elderly or infirm and was exposed to a hot environment. However, reporting of hyperthermia on a death certificate depends on the criteria of individual MEs or coroners. This article describes three case reports of heat-related deaths in other parts of the United States in 1993, summarizes risk factors for this problem, and reviews measures to prevent heat-related illness.

Case 1. On June 2, a 1-year-old infant was left sleeping for approximately 75 minutes in the back seat of an automobile with the windows closed. The child died from hyperthermia attributable to exposure to a hot environment.

Case 2. On July 7, a 48-year-old woman was found unconscious at her kitchen table in her mobile home and was pronounced dead on arrival at a local emergency department. Rectal temperature, measured at the emergency department, was 108 F (42 C) following a 20-minute ride in an air-conditioned ambulance. At the time the decedent was discovered, all the windows in her home were closed and all fans were turned off. The room temperature was approximately 120 F (48.8 C). She had been dehydrated the previous day when she presented to a local health department for a prescheduled visit. The direct cause of death was hyperthermia.

Case 3. On July 8, a 68-year-old man was found in a slightly decomposed state in his apartment. He was last seen alive on July 5. Room temperature exceeded 100 F (38 C). Although the direct cause of death was atherosclerotic heart disease, hyperthermia was considered a contributing factor.

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Editorial note: During 1979–1988, 4523* deaths in the United States were attributed to excessive heat exposure, and in 1980 (a year with a severe heat wave), 1700 heat-related deaths were reported†. Mortality from all causes increases during heat waves, and excessive heat is an important contributing factor to deaths from other causes, particularly among the elderly (*1*). However, because deaths attributable to heat-related illness vary according to criteria used by individual MEs and coroners, a standard definition is needed to accurately assess these deaths. The current heat wave in the eastern part of the United States underscores the need for health-care

*Underlying cause of death attributed to excessive heat exposure and coded E-900 according to the *International Classification of Diseases, Ninth Revision*.

†These data were obtained from the Compressed Mortality File (CMF), provided by CDC's National Center for Health Statistics. It contains information from death certificates filed in the 50 states and the District of Columbia that have been prepared in accordance with external cause codes from the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM). CDC's Wide- ranging ONline Data for Epidemiologic Research (WONDER) computerized information system was used to access CMF data.

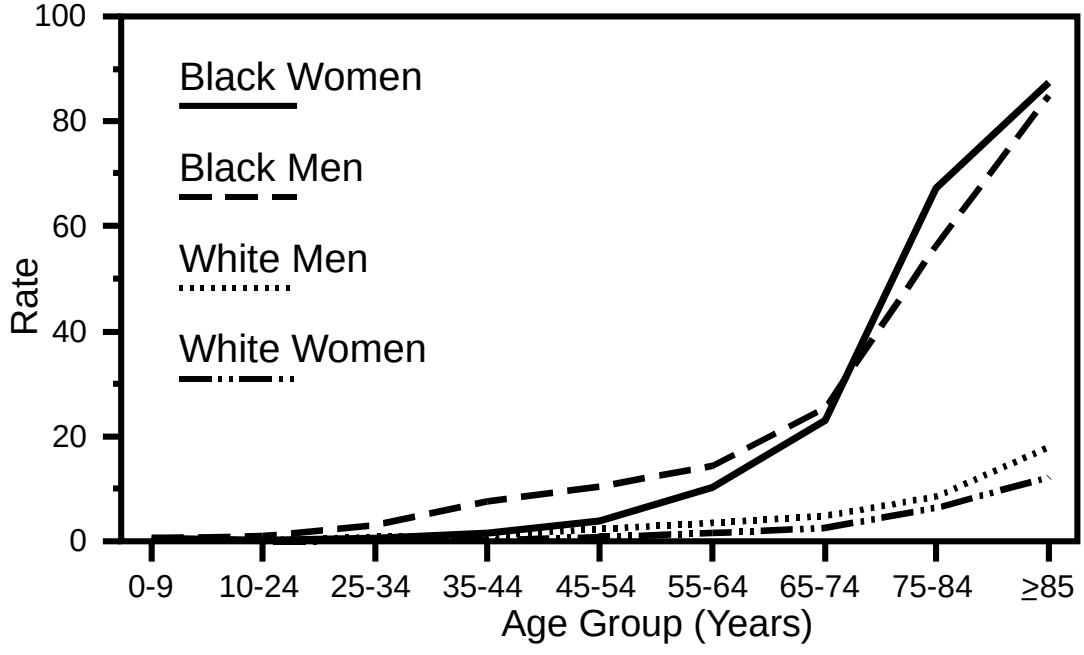
Heat-Related Deaths — Continued

providers, public health agencies, and the public to recognize risk factors for heat-related illness and to implement measures to lower the risk for these illnesses.

Based on data for the United States for 1979–1988, the risk for death from excessive exposure to heat varied by age, sex, and race (Figure 1). This risk was higher among men and non-Hispanic blacks, although these rates were not adjusted for potential risk factors, such as socioeconomic status (*2*). Regardless of sex or race, persons aged ≥65 years were more susceptible to the adverse effects of heat than were younger persons, and heat-related death rates increased with age: the risk of heat-related mortality for persons aged ≥85 years was 3.6 times that for persons aged 65–74 years.

Persons at greatest risk for heat-related illness include the very young, the elderly, and those who overexert themselves in hot environments, either at work or during recreational activities. However, any person is at risk for fatal heatstroke if sufficiently exposed. Because young children (particularly infants), the elderly, and the immobile may be unable to obtain adequate fluids or to avoid hot environments, they are at greater risk for heat exhaustion or heatstroke (*3*). The use of certain drugs, such as neuroleptics or medications with anticholinergic effects, may also increase the risk for heat-related illness (*3*). Healthy adults who are unacclimatized to the heat and who work or exercise vigorously outdoors, who fail to rest frequently, or who do not drink enough fluids are also at high risk. Excessive alcohol consumption may cause dehydration and result in heat-related illness (*3*).

FIGURE 1. Rate* of heat-related deaths†, by age and race§ — United States, 1979–1988



*Per 100,000 population.
†Underlying cause of death attributed to excessive heat exposure and coded E-900 according to the *International Classification of Diseases, Ninth Revision*.
§Numbers for other racial/ethnic groups were too small for meaningful analysis.

Heat-Related Deaths — Continued

Heatstroke, the most serious heat-related illness, is a medical emergency. It is characterized by a body temperature ≥105 F (40.5 C) and may include disorientation, delirium, and coma. Onset of heatstroke can be rapid: clinical status can change from apparently normal to seriously ill within minutes. Treatment of heatstroke involves the rapid lowering of body temperature (e.g., ice bath) (*3*). Heat exhaustion—a milder form of heat-related illness that may develop after several days of high temperatures and inadequate or unbalanced replacement of fluids and electrolytes—is characterized by dizziness, weakness, and fatigue and may require hospitalization.

The most effective measures for preventing heat-related illness include reducing physical activity, drinking additional liquids, and increasing the amount of time spent in an air-conditioned environment (*3*). Physically active persons can reduce risk for heat-related illness by scheduling exercise during the cooler parts of the day and by drinking additional nonalcoholic fluids.

The use of air conditioning will reduce the risk for heatstroke, even if it is available only for part of the day. The elderly should be encouraged and assisted in taking advantage of such environments in private or in public places (e.g., shopping malls, public libraries, and heat-wave shelters).

Salt tablets are not recommended and may be potentially dangerous for most persons (*2*). Persons for whom fluid restriction has been prescribed or who are taking diuretic medications should alter their fluid intake patterns only if advised by their physicians. Although the use of fans may increase comfort at low temperatures, fans are not protective against heatstroke at dangerously high temperatures. Fan distribution, as part of heat-wave relief, is not recommended (*4,5*), and persons without home air conditioners should seek shelter in an air-conditioned environment (*3*).

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Creutzfeldt-Jakob Disease in Patients Who Received a Cadaveric Dura Mater Graft — Spain, 1985–1992

In 1987, CDC and the Food and Drug Administration (FDA) investigated a case of Creutzfeldt-Jakob disease (CJD) in a 28-year-old woman in the United States; the patient had onset of CJD 19 months after an operation in which she received an imported, commercially prepared, cadaveric dura mater graft (LYODURA®, processed by B. Braun Melsungen AG of the Federal Republic of Germany) (*1,2*). The report of this investigation alerted medical personnel and the public about a possible increased risk for CJD in recipients of these human tissue grafts. Recently, CDC was notified of four patients with CJD who had undergone dura mater repair with the aid of LYODURA®.

Creutzfeldt-Jakob Disease — Continued

All four patients had neurosurgery at a regional hospital in Spain during April 1983–January 1984 (*3,4*). This report describes these four cases.

Case 1. In 1985, a 19-year-old man was hospitalized for gait ataxia, blurred vision, dysarthria, and dysmetria 16 months after surgical resection of a cystic cerebellar astrocytoma that included closure of the dura mater using LYODURA®. During the 2 weeks following hospitalization, he became progressively demented, developed myoclonic jerks, and had an electroencephalogram (EEG) that revealed diffuse slow activity with periodic paroxysms of bilateral spike waves. A right frontal cerebral biopsy showed spongiform changes consistent with CJD. He died in 1986, 21 months after clinical onset.

Case 2. In 1987, a 57-year-old woman was hospitalized for gait ataxia, dysarthria, dizziness, and bilateral hypertonus 43 months following a posterior fossa decompression and cervical vertebrae level 1 laminectomy, which included placement of a LYODURA® graft to correct an Arnold-Chiari malformation and syringomyelia. Two weeks after hospitalization, she became demented and showed facial and limb myoclonic movements. A right frontal cerebral biopsy was consistent with CJD. She died in 1989, 25 months after clinical onset.

Case 3. In 1991, an 18-year-old man was hospitalized for ataxia, dysmetria, dysarthria, and generalized hyperreflexia 79 months after undergoing a posterior fossa craniectomy for removal of a cerebellar astrocytoma; a LYODURA® graft was used to close the dura mater. During the 2 weeks following hospitalization, he was mute with decorticate posture and myoclonic movements of all four limbs. An EEG showed the characteristic triphasic waves of CJD; a cerebral biopsy was consistent with CJD. He died in 1992, 3 months after clinical onset.

Case 4. In 1992, a 34-year-old man reported dizziness and slurred speech 105 months after undergoing a posterior fossa decompression in which a LYODURA® graft was used to repair an Arnold-Chiari malformation and syringomyelia. He also had ataxia, nystagmus, mild hyperreflexia, and bilateral pale optic discs. He rapidly progressed to mutism, and decorticate posturing with myoclonic movements in all four limbs. An EEG revealed periodic activity; a brain biopsy was consistent with CJD. As of June 1993, the patient was still hospitalized.

General characteristics. None of these patients had received growth or other hormones derived from cadaveric sources, had undergone prior surgical procedures, or had a familial history of CJD. From January 1983 through December 1984, of 1052 persons who underwent neurosurgical procedures at this hospital, 37 (including case-patients 1–4) had placement of a LYODURA® graft. No other episodes of CJD have been noted among these 1052 patients. Although records of LYODURA® lot numbers were not available at the hospital, the manufacturer indicated that the grafts were not from lot number 2105, which was implicated in the initially investigated LYODURA-associated CJD patient in the United States.

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Editorial Note: CJD is a rapidly fatal, dementing neurologic illness. It is characterized by cerebral spongiform changes and transmissibility when central nervous system tissue from a patient is inoculated into susceptible animal hosts. The infectivity of CJD has been hypothesized to be related to a novel self-replicating protein (*5*). In the

Creutzfeldt-Jakob Disease — Continued

United States and Europe, the estimated crude annual incidence is one case per million persons (*6*). For persons aged <30 years, however, the estimated incidence is less than one case per 200 million (*7*). Iatrogenic transmission has been reported following use of infective cadaveric materials (e.g., corneal transplant), neurosurgical procedures, contaminated EEG depth electrodes, or administration of growth and other hormones derived from cadaveric pituitaries (*8*).

The first report of LYODURA®-associated CJD included a description of differences between the processing of LYODURA® and similar products and suggested that, in the United States, the risk for transmission of CJD using LYODURA® was higher than that from other dura mater products (*1,2*). Following the first report, the FDA issued a safety alert recommending disposal of specified packages of LYODURA® (*9*). Subsequently, representatives of B. Braun Melsungen AG reported that their procedures for collection and processing of dura after May 1, 1987, were revised to reduce the risk for CJD transmission (*6,7*).

Consistent with a subsequently reduced risk for CJD transmission, there have been no reports of CJD in patients who received LYODURA® processed after May 1987. However, CJD has been reported in eight patients from outside the United States, including the four described in this report, who received LYODURA® products processed before May 1987 (*6,10*). A probable 10th case of LYODURA®-associated CJD recently has been reported in a 29-year-old patient in the United States who had placement of a dural graft during the correction of an Arnold-Chiari malformation in 1985 and died in 1992 (CDC, unpublished data, 1993). CJD also has been reported in two persons from Italy who received dura allografts from other manufacturers (*6*).

The most stringent donor screening cannot assure the exclusion of donors with prepatent CJD. Therefore, surgeons should confirm that allogenic dura mater they use is handled according to strict guidelines such as those established by the American Association of Tissue Banks and the Southeastern Organ Procurement Foundation (*11*); surgeons may want to consider the alternative use of autologous fascia lata, temporalis fascia, or of synthetic substitutes.

The cases described in this report indicate that recipients of contaminated grafts may remain at risk for CJD at least 8 years following receipt of grafts. Patients who have rapidly progressive dementing illnesses consistent with CJD and who have received an allograft should be reported through their respective local or state health departments to CDC's Division of Viral and Rickettsial Diseases, National Center for Infectious Diseases, telephone (404) 639-3091.

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