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Update: Treatment of Cryptosporidiosis in Patients with Acquired Immunodeficiency Syndrome (AIDS)

In November 1982, 21 patients with acquired immunodeficiency syndrome (AIDS) and severe, protracted diarrhea caused by cryptosporidiosis were reported; the report concluded that no effective treatment for cryptosporidiosis was known at that time (*1*). Since then, 91 additional AIDS patients with chronic cryptosporidiosis have been reported to CDC. Although no therapy has been consistently effective in treating them, preliminary reports suggest that a few may have responded to treatment with spiramycin (Rovamycine,* Rhône-Poulenc Pharma, Montreal) or the combination of quinine and clindamycin.

Since December 1982, physicians at the University of Miami, Florida, have used spiramycin to treat seven AIDS patients with chronic cryptosporidiosis; six other AIDS patients with cryptosporidiosis have been treated with spiramycin at five other institutions; and one non-AIDS patient with chronic cryptosporidiosis associated with a bone marrow transplant has received the drug. Thirteen of the 14 patients were adults; they received 1 g of spiramycin orally three or four times a day. The 14th patient, a 2-year-old child, received 500 mg orally twice a day. No adverse effects were attributed to the drug.

Three of the 13 AIDS patients were apparently cured after 3-4 weeks of spiramycin therapy (i.e., all three improved symptomatically, and intestinal biopsies and three successive stool examinations after therapy were negative). Follow-up 6-7 months after discontinuation of spiramycin revealed that all three remained asymptomatic. Two have subsequently died from causes related to their underlying immunodeficiency—one with Kaposi's sarcoma, the other with *Pneumocystis carinii* pneumonia.

In an additional three AIDS patients, gastrointestinal symptoms improved rapidly with spiramycin (in two cases, within 48 hours of starting the drug), but these patients continued to have *Cryptosporidium* in their stools. Spiramycin was continued for variable periods of time, but when therapy was stopped, diarrhea in each patient promptly recurred. On reinitiation of spiramycin, two of the three again improved, but the third continued to have severe diarrhea and has since died. One of the two surviving patients had *Cryptosporidium* detected in his stool at weekly intervals for the first 3½ months of therapy. The patient recently had three negative stools, and spiramycin was stopped; he now has been off therapy for 2 weeks and remains asymptomatic.

The remaining seven AIDS patients did not respond symptomatically or parasitologically to spiramycin. Three, however, died within 2-7 days after starting spiramycin. None of the deaths was attributed to spiramycin.

A non-AIDS patient with chronic cryptosporidiosis, acquired after receiving a bone marrow transplant, also improved with spiramycin therapy. She began spiramycin after suf-

*Use of trade names is for identification only and does not imply endorsement by the Public Health Service or the U.S. Department of Health and Human Services.

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fering from severe, watery diarrhea and abdominal cramps for 6 weeks; within 24 hours, her cramps had resolved and her diarrhea had improved, and 2 weeks later, she was having one bowel movement a day. After 3 weeks of therapy, a stool examination was negative for *Cryptosporidium*.

CDC has also received six reports of AIDS patients and one bone marrow transplant patient with cryptosporidiosis who were treated with a combination of quinine and clindamycin, both given orally. Two patients did not respond after 7-14 days of therapy. In three others, the drugs were discontinued because of adverse effects; one developed a severe rash; another, severe vomiting; the third, thrombocytopenia. Symptoms improved in two of these three patients during the first few days of therapy. The sixth patient had acute cholecystitis and diarrhea associated with *Cryptosporidium* of the cystic duct and intestines. He received 300 mg of clindamycin and 250 mg of quinine, given orally four times a day. Within 2 days of initiating therapy, the patient's diarrhea resolved, but stool examinations after therapy continued to show occasional *Cryptosporidium*. A seventh patient, who developed chronic cryptosporidiosis after receiving a bone marrow transplant, also received oral quinine and clindamycin; the patient showed no clinical improvement despite 2 weeks of therapy.

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Editorial Note: *Cryptosporidium* is a protozoan parasite that causes severe, protracted diarrhea in immune suppressed patients. The first patient with human cryptosporidiosis was reported in 1976, and before 1982, only seven cases of human cryptosporidiosis had been published. During 1982 and 1983, however, the number of reported cases has increased steadily (*2*).

The case reports described here are the first to offer encouragement in the treatment of cryptosporidiosis in immune suppressed patients. However, these reports must be viewed cautiously for several reasons. Most of the patients have had no response to spiramycin or the combination of clindamycin and quinine, and many of the patients who have responded symptomatically have not had parasitologic cures. Furthermore, treatment with clindamycin and quinine was associated frequently with adverse effects. Little is known about spiramycin's antiprotozoal activity. There are no published reports evaluating the efficacy of spiramycin against cryptosporidiosis in animals, and preliminary results by investigators at Auburn University, Alabama, suggest that spiramycin does not inhibit *Cryptosporidium* growth in tissue culture (*3*). Spiramycin is used in Europe and Canada to treat infections caused by another protozoan parasite, *Toxoplasma gondii*, but studies of spiramycin's efficacy for human toxoplasmosis have not included appropriate control groups, and animal studies have produced equivocal results (*4-7*).

Spiramycin is a macrolide antibiotic with an antimicrobial activity similar to erythromycin and clindamycin. It has been used in Europe and Canada for over 20 years to treat bacterial infections. Serious adverse effects from spiramycin are apparently rare, and no drug-associated deaths have been reported. Two patients have been reported who complained of nausea, sweating, giddiness, and paresthesia 1 hour after a single oral dose of 3 g; the symptoms subsided spontaneously within an hour (*8*). Mild to moderate diarrhea, including bloody diarrhea in two cases, has been reported in patients receiving various doses of spiramycin (*8-12*). Other reports of adverse reactions include one patient who developed a mild rash and others who developed contact dermatitis after handling spiramycin in animal feed (*13-16*).

The U.S. Food and Drug Administration (FDA) has not approved spiramycin for routine use, and therefore, the drug is not commercially available in the United States. Physicians in the

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United States who wish to obtain spiramycin should contact the FDA's Division of Anti-infective Drug Products, telephone (301) 443-4310.

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Japanese Encephalitis: Report of a World Health Organization Working Group

Japanese encephalitis (JE) is a public health problem of increasing concern to countries in Southeast Asia and the Western Pacific because of the occurrence of thousands of cases over the past decade, with high case-fatality rates and expansion into new areas.

A World Health Organization (WHO) Working Group on the prevention and control of JE was convened in Tokyo, Japan, from December 19, to December 21, 1983, to review the current epidemiology; recommend ways of strengthening surveillance and control of the disease; and develop collaborative studies for vaccine development, production, control, and utilization.

Epidemiology: JE has changed epidemiologically during the past 10 years. The disease has recently been recognized in new areas and has recurred in previously endemic areas. In the Republic of Korea, after a decade of very low incidence, a resurgence was noted in 1982. Since 1978, JE has appeared as a new and major entity in the plains region of southern Nepal. It has been focally endemic in a few states of southern India for decades. In 1978, however, JE was recognized for the first time in Bihar, Uttar Pradesh, and West Bengal States in the north. This focus is contiguous to the affected area in Nepal.

Since 1966, JE has been uncommon in Japan, in part because of widespread vaccination

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of children 3-15 years of age and a decline in the vector population, *Culex tritaeniorhynchus*. In China, the disease is prevalent in all provinces except Xinjiang, Chenghai, and Tibet; over 10,000 cases are reported annually, with a case-fatality rate of approximately 10%. In Thailand, JE has become an increasingly reported disease over the past 10 years, primarily in the north and northeast regions. The attack rate and case-fatality rate were higher among children than adults. In Burma, fewer than 100 cases of JE are reported each year and confined mostly to children in tribal areas.

Vaccines: Formalin-inactivated vaccines have been manufactured and used in Japan and China for many years, and during the last decade, in the Republic of Korea. The Japanese and Korean vaccines are made in adult mouse brain; the Chinese vaccine, in primary hamster kidney tissue culture. Presently, the vaccines are evaluated in the countries of origin by different methods. A live, attenuated vaccine developed in China has undergone extensive field trials in humans and horses. The Working Group requested that WHO consider formulating requirements for JE vaccine and for establishing a reference standard preparation. The potency of candidate vaccines would be assessed in collaborative studies in terms of international (WHO) antigenic units. Field trials could be conducted under the auspices of WHO.

The Collaborating Centre for Arbovirus Reference and Research, Tokyo, will be the focal point for the above-mentioned studies, supported by the WHO network of Collaborating Centres.

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TABLE I. Summary—cases specified notifiable diseases, United States

Disease	9th Week Ending			Cumulative, 9th Week Ending		
	March 3, 1984	March 5, 1983	Median 1979-1983	March 3, 1984	March 5, 1983	Median 1979-1983
Acquired Immunodeficiency Syndrome (AIDS)	17	N	N	497	N	N
Aseptic meningitis	72	96	73	710	751	582
Encephalitis: Primary (arthropod-borne & unspec.)	13	15	12	104	148	135
Post-infectious	-	2	2	5	8	14
Gonorrhea: Civilian	14,074	17,930	17,957	138,805	158,901	162,798
Military	284	583	583	3,318	4,414	4,895
Hepatitis: Type A	438	507	537	3,743	4,186	4,186
Type B	426	404	384	3,678	3,591	3,099
Non A, Non B	57	57	N	546	501	N
Unspecified	112	168	200	1,040	1,233	1,677
Legionellosis	10	17	N	73	99	N
Leprosy	6	1	3	35	41	33
Malaria	17	12	12	92	109	121
Measles: Total*	5	72	72	211	160	385
Indigenous	4	70	N	189	131	N
Imported	1	2	N	22	29	N
Meningococcal infections: Total	84	57	83	539	516	573
Civilian	84	56	81	539	506	570
Military	-	1	-	-	10	3
Mumps	93	92	142	604	694	939
Pertussis	37	30	23	283	204	186
Rubella (German measles)	16	36	76	88	157	424
Syphilis (Primary & Secondary): Civilian	468	619	568	4,849	5,888	5,274
Military	3	10	10	55	92	76
Toxic Shock syndrome	11	8	N	56	72	N
Tuberculosis	327	467	512	3,141	3,475	3,921
Tularemia	6	3	3	15	25	16
Typhoid fever	2	5	8	42	61	63
Typhus fever, tick-borne (RMSF)	2	-	-	9	10	10
Rabies, animal	82	119	93	658	851	810

TABLE II. Notifiable diseases of low frequency, United States

	Cum. 1984		Cum. 1984
Anthrax	-	Plague	2
Botulism: Foodborne (Ohio 1)	2	Poliomyelitis: Total	-
Infant (Calif. 2)	9	Paralytic	-
Other	1	Psittacosis	10
Brucellosis	19	Rabies, human	-
Cholera	-	Tetanus	3
Congenital rubella syndrome	-	Trichinosis (N.J. 3)	5
Diphtheria	-	Typhus fever, flea-borne (endemic, murine)	4
Leptospirosis	3		

*One of the 5 reported cases for this week was imported from a foreign country or can be directly traceable to a known internationally imported case within two generations.

TABLE III. Cases of specified notifiable diseases, United States, weeks ending March 3, 1984 and March 5, 1983 (9th Week)

Reporting Area	AIDS	Aseptic Meningitis	Encephalitis		Gonorrhea (Civilian)		Hepatitis (Viral), by type				Legionellosis	Leprosy
			Primary	Post-infectious			A	B	NA,NB	Unspecified		
	Cum. 1984	1984	Cum. 1984	Cum. 1984	Cum. 1984	Cum. 1983	1984	1984	1984	1984	1984	Cum. 1984
UNITED STATES	497	72	104	5	138,805	158,901	438	426	57	112	10	35
NEW ENGLAND	21	-	5	-	4,639	3,934	11	35	-	8	2	1
Maine	-	-	-	-	178	236	1	-	-	-	-	-
N.H.	-	-	2	-	101	117	2	4	-	-	-	-
Vt.	-	-	-	-	66	69	1	-	-	-	-	-
Mass.	13	-	3	-	1,753	1,713	3	18	-	8	-	1
R.I.	-	-	-	-	281	216	-	-	-	-	-	-
Conn.	8	-	-	-	2,260	1,583	4	13	-	-	2	-
MID ATLANTIC	248	4	11	-	18,083	20,020	53	48	1	4	-	2
Upstate N.Y.	23	2	4	-	2,808	2,782	6	8	-	1	-	2
N.Y. City	202	1	-	-	7,856	8,528	26	13	-	2	-	-
N.J.	22	-	3	-	2,548	3,683	U	U	U	U	-	-
Pa.	1	1	4	-	4,871	5,027	21	27	1	1	-	-
E.N. CENTRAL	16	15	20	1	17,426	22,375	66	53	4	7	3	3
Ohio	8	4	8	1	4,833	5,585	31	17	-	2	3	1
Ind.	-	1	1	-	2,281	2,673	7	5	-	3	-	-
Ill.	7	5	2	-	2,565	6,128	11	4	-	1	-	-
Mich.	1	5	7	-	5,600	6,055	17	27	4	1	-	2
Wis.	-	-	2	-	2,147	1,934	-	-	-	-	-	-
W.N. CENTRAL	1	1	3	-	6,356	7,431	10	12	3	2	1	-
Minn.	-	1	-	-	914	1,160	2	2	2	-	-	-
Iowa	1	-	2	-	776	761	-	5	-	-	-	-
Mo.	-	-	-	-	2,798	3,485	2	3	-	2	1	-
N. Dak.	-	-	-	-	82	76	-	-	-	-	-	-
S. Dak.	-	-	-	-	220	206	6	1	-	-	-	-
Nebr.	-	-	-	-	435	392	-	-	-	-	-	-
Kans.	-	-	1	-	1,131	1,351	-	1	1	-	-	-
S. ATLANTIC	46	14	22	4	36,119	40,289	28	93	16	9	2	2
Del.	1	1	1	-	604	810	-	3	1	-	-	-
Md.	15	1	4	-	4,791	5,177	1	12	-	-	-	-
D.C.	6	1	-	-	2,679	2,814	-	5	-	-	-	-
Va.	2	1	8	3	3,502	3,489	2	7	4	1	-	1
W. Va.	-	2	3	-	391	396	1	2	-	-	-	-
N.C.	-	1	3	1	5,795	5,650	3	12	-	4	-	-
S.C.	-	-	1	-	3,273	4,099	-	5	-	-	1	-
Ga.	-	1	2	-	7,083	8,171	7	19	1	-	1	-
Fla.	22	6	-	-	8,001	9,683	14	28	10	4	-	1
E.S. CENTRAL	4	6	6	-	12,091	14,107	2	28	2	2	1	-
Ky.	2	1	-	-	1,491	1,814	1	4	1	-	-	-
Tenn.	-	2	2	-	4,829	5,286	1	19	1	2	-	-
Ala.	1	3	4	-	4,001	4,539	-	2	-	-	-	-
Miss.	1	-	-	-	1,770	2,468	-	3	-	-	1	-
W.S. CENTRAL	9	7	8	-	19,426	22,154	70	44	-	60	-	2
Ark.	-	-	-	-	1,626	1,839	1	2	-	3	-	-
La.	5	1	2	-	4,679	3,469	14	10	-	-	-	-
Okla.	1	-	-	-	2,148	2,683	4	5	-	1	-	-
Tex.	3	6	6	-	10,973	14,163	51	27	-	56	-	2
MOUNTAIN	4	4	2	-	4,295	4,731	53	18	9	4	1	4
Mont.	-	1	-	-	226	245	2	-	1	-	1	-
Idaho	-	-	-	-	191	242	-	-	-	-	-	-
Wyo.	-	-	-	-	116	147	1	-	-	-	-	-
Colo.	-	1	1	-	1,088	1,356	22	6	2	2	-	-
N. Mex.	-	-	-	-	553	638	10	1	4	1	-	-
Ariz.	4	1	-	-	1,145	1,093	7	9	2	-	-	4
Utah	-	1	1	-	241	226	9	2	-	-	-	-
Nev.	-	-	-	-	735	784	2	-	-	1	-	-
PACIFIC	148	21	27	-	20,370	23,860	145	95	22	16	-	21
Wash.	3	-	-	-	1,300	1,721	1	1	1	2	-	1
Oreg.	-	-	-	-	1,279	1,162	19	8	2	-	-	1
Calif.	143	19	27	-	16,956	19,962	124	81	19	14	-	15
Alaska	-	-	-	-	521	536	-	1	-	-	-	-
Hawaii	2	2	-	-	314	479	1	4	-	-	-	4
Guam	-	U	-	-	-	44	U	U	U	U	U	-
P.R.	-	1	-	-	583	542	14	15	-	20	-	-
V.I.	-	-	-	-	73	50	-	-	-	-	-	-
Pac. Trust Terr.	-	U	-	-	-	-	U	U	U	U	U	-

N: Not notifiable U: Unavailable

TABLE III. (Cont.'d). Cases of specified notifiable diseases, United States, weeks ending March 3, 1984 and March 5, 1983 (9th Week)

Reporting Area	Malaria	Measles (Rubeola)					Menin-gococcal Infections	Mumps		Pertussis			Rubella		
		Indigenous		Imported *		Total									
	Cum. 1984	1984	Cum. 1984	1984	Cum. 1984	Cum. 1983	Cum. 1984	1984	Cum. 1984	1984	Cum. 1984	Cum. 1983	1984	Cum. 1984	Cum. 1983
UNITED STATES	92	4	189	1	22	160	539	93	604	37	283	204	16	88	157
NEW ENGLAND	11	-	-	-	-	-	45	3	27	-	6	11	6	8	1
Maine	-	-	-	-	-	-	1	1	8	-	-	-	-	1	-
N.H.	-	-	-	-	-	-	4	-	3	-	1	3	-	-	-
Vt.	1	-	-	-	-	-	14	-	1	-	4	2	-	-	1
Mass.	5	-	-	-	-	-	14	1	11	-	-	5	6	7	-
R.I.	1	-	-	-	-	-	3	-	1	-	1	1	-	-	-
Conn.	4	-	-	-	-	-	9	1	3	-	-	-	-	-	-
MID ATLANTIC	6	-	3	-	1	3	61	6	85	1	18	44	1	1	9
Upstate N.Y.	2	-	-	-	-	1	23	2	21	1	10	23	-	-	6
N.Y. City	-	-	3	-	-	1	1	-	3	-	-	5	-	-	2
N.J.	2	-	-	-	1	1	17	3	53	-	-	6	1	1	1
Pa.	2	-	-	-	-	-	20	1	8	-	8	10	-	-	-
E.N. CENTRAL	10	2	106	1	2	68	80	43	214	10	81	54	2	11	22
Ohio	4	1	1	1†	2	1	34	25	65	3	15	24	-	-	1
Ind.	-	-	1	-	-	32	10	1	16	6	47	3	-	-	-
Ill.	1	-	15	-	-	30	11	3	51	-	6	19	-	8	7
Mich.	3	1	89	-	-	5	18	14	66	1	5	2	1	2	4
Wis.	2	-	-	-	-	-	7	-	16	-	8	6	1	1	10
W.N. CENTRAL	5	-	-	-	-	-	32	4	29	9	54	9	2	7	10
Minn.	-	-	-	-	-	-	2	-	1	-	2	-	-	-	3
Iowa	1	-	-	-	-	-	13	2	9	-	3	2	-	-	-
Mo.	3	-	-	-	-	-	10	-	4	8	9	2	-	-	-
N. Dak.	-	-	-	-	-	-	-	-	1	-	-	-	-	1	-
S. Dak.	-	-	-	-	-	-	1	-	-	-	-	-	-	-	-
Nebr.	-	-	-	-	-	-	2	-	1	-	-	-	-	-	-
Kans.	1	-	-	-	-	-	4	2	13	1	40	5	2	6	7
S. ATLANTIC	12	2	2	-	2	42	135	7	51	3	33	31	2	9	12
Del.	2	-	-	-	-	-	1	-	2	-	-	-	-	-	-
Md.	4	-	-	-	-	1	10	1	10	-	1	4	-	-	-
D.C.	-	-	-	-	-	-	2	-	-	-	-	-	-	-	-
Va.	2	-	-	-	1	2	11	-	2	1	6	8	-	-	1
W. Va.	-	-	-	-	-	-	2	2	8	-	3	2	-	-	-
N.C.	1	-	-	-	-	-	20	3	8	1	13	-	-	-	-
S.C.	1	-	-	-	-	3	14	-	1	-	1	2	-	-	-
Ga.	-	-	-	-	-	2	31	-	3	-	2	12	-	1	5
Fla.	2	2	2	-	1	34	44	1	17	1	7	3	2	8	6
E.S. CENTRAL	-	-	-	-	2	-	23	2	10	-	2	3	-	-	3
Ky.	-	-	-	-	-	-	4	-	3	-	1	1	-	-	3
Tenn.	-	-	-	-	2	-	9	2	2	-	1	2	-	-	-
Ala.	-	-	-	-	-	-	6	-	3	-	-	-	-	-	-
Miss.	-	-	-	-	-	-	4	-	2	-	-	-	-	-	-
W.S. CENTRAL	3	-	41	-	-	10	65	7	28	9	27	22	-	11	24
Ark.	-	-	-	-	-	10	5	3	3	-	9	1	-	1	-
La.	-	-	-	-	-	-	15	-	-	-	1	2	-	-	-
Okla.	2	-	-	-	-	-	10	N	N	9	16	8	-	-	-
Tex.	1	-	41	-	-	-	35	4	25	-	1	11	-	10	24
MOUNTAIN	4	-	20	-	8	1	23	6	60	-	33	23	-	3	6
Mont.	-	-	-	-	-	-	1	1	2	-	18	1	-	-	1
Idaho	-	-	-	-	-	-	3	-	4	-	1	1	-	1	-
Wyo.	-	-	-	-	-	-	-	-	1	-	-	-	-	-	1
Colo.	1	-	-	-	-	1	10	-	3	-	11	16	-	-	-
N. Mex.	-	-	-	-	8	-	3	N	N	-	2	4	-	-	-
Ariz.	1	-	-	-	-	-	3	4	48	-	-	-	-	-	3
Utah	2	-	20	-	-	-	3	1	2	-	1	1	-	2	1
Nev.	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PACIFIC	41	-	17	-	7	36	75	15	100	5	29	7	3	38	70
Wash.	2	-	5	-	-	1	7	2	15	-	6	1	-	-	-
Oreg.	1	-	-	-	-	2	12	N	N	-	4	-	-	-	5
Calif.	35	-	12	-	5	32	54	12	80	2	13	6	3	37	65
Alaska	-	-	-	-	-	-	2	-	3	-	-	-	-	-	-
Hawaii	3	-	-	-	2	1	-	1	2	3	6	-	-	1	-
Guam	-	U	-	U	-	-	-	U	-	U	-	-	U	-	-
P.R.	2	-	-	-	-	18	2	-	27	-	-	2	-	1	1
V.I.	-	-	-	-	-	5	-	-	-	-	-	-	-	-	1
Pac. Trust Terr.	-	U	-	U	-	-	-	U	-	U	-	-	U	-	-

*For measles only, imported cases includes both out-of-state and international importations.

N: Not notifiable U: Unavailable †International §Out-of-state

TABLE III. (Cont.'d). Cases of specified notifiable diseases, United States, weeks ending March 3, 1984 and March 5, 1983 (9th Week)

Reporting Area	Syphilis (Civilian) (Primary & Secondary)		Toxic-shock Syndrome	Tuberculosis		Tula-remia	Typhoid Fever	Typhus Fever (Tick-borne) (RMSF)	Rabies, Animal
	Cum. 1984	Cum. 1983	1984	Cum. 1984	Cum. 1983	Cum. 1984	Cum. 1984	Cum. 1984	Cum. 1984
UNITED STATES	4,849	5,888	11	3,141	3,475	15	42	9	658
NEW ENGLAND	109	147	-	91	75	1	-	-	3
Maine	1	1	-	4	7	-	-	-	3
N.H.	1	3	-	8	6	-	-	-	-
Vt.	-	1	-	3	1	-	-	-	-
Mass.	65	101	-	43	33	1	-	-	-
R.I.	5	3	-	11	7	-	-	-	-
Conn.	37	38	-	22	21	-	-	-	-
MID ATLANTIC	658	701	2	591	700	-	8	-	47
Upstate N.Y.	44	60	-	99	115	-	4	-	2
N.Y. City	372	403	-	234	273	-	1	-	-
N.J.	135	134	-	116	163	-	3	-	-
Pa.	107	104	2	142	149	-	-	-	45
E.N. CENTRAL	157	358	3	422	519	-	5	1	21
Ohio	37	93	2	97	81	-	2	1	2
Ind.	34	38	-	43	79	-	1	-	4
Ill.	30	161	-	155	250	-	-	-	9
Mich.	39	50	1	105	82	-	-	-	1
Wis.	17	16	-	22	27	-	2	-	5
W.N. CENTRAL	82	71	2	75	122	4	2	2	97
Minn.	15	35	1	10	18	-	2	-	11
Iowa	8	2	1	11	17	-	-	-	23
Mo.	47	25	-	33	69	4	-	2	6
N. Dak.	-	-	-	3	-	-	-	-	18
S. Dak.	-	-	-	1	7	-	-	-	23
Nebr.	4	1	-	7	2	-	-	-	5
Kans.	8	8	-	10	9	-	-	-	11
S. ATLANTIC	1,521	1,511	2	742	636	1	3	1	241
Del.	4	10	-	5	1	-	-	-	-
Md.	65	86	-	88	57	-	-	-	172
D.C.	55	57	-	19	22	-	1	-	-
Va.	80	114	-	57	42	-	1	-	40
W. Va	7	4	-	25	32	-	-	-	4
N.C.	161	149	1	136	65	-	-	-	-
S.C.	150	123	-	96	62	-	-	-	-
Ga.	259	269	-	85	117	1	-	-	24
Fla.	740	699	1	231	238	-	1	1	1
E.S. CENTRAL	345	404	-	287	343	-	2	3	34
Ky.	17	23	-	74	96	-	-	-	8
Tenn.	79	111	-	89	98	-	2	1	17
Ala.	120	162	-	103	87	-	-	2	9
Miss.	129	108	-	21	62	-	-	-	-
W.S. CENTRAL	1,161	1,449	-	258	341	4	2	1	133
Ark.	48	23	-	11	18	3	-	1	13
La.	245	281	-	41	62	-	1	-	-
Okla.	29	42	-	35	47	1	-	-	14
Tex.	839	1,103	-	171	214	-	1	-	106
MOUNTAIN	108	123	-	53	101	3	2	-	18
Mont.	-	2	-	1	8	-	1	-	9
Idaho	5	1	-	3	7	-	-	-	-
Wyo.	1	2	-	-	2	-	-	-	-
Colo.	20	29	-	6	6	-	-	-	-
N. Mex.	13	47	-	15	17	-	1	-	4
Ariz.	45	20	-	24	46	1	-	-	5
Utah	4	6	-	3	8	2	-	-	-
Nev.	20	16	-	1	7	-	-	-	-
PACIFIC	708	1,124	2	622	638	2	18	1	64
Wash.	12	42	-	21	39	-	1	-	-
Oreg.	22	18	-	27	29	1	-	1	-
Calif.	656	1,038	2	515	522	1	14	-	62
Alaska	1	6	-	18	6	-	1	-	2
Hawaii	17	20	-	41	42	-	2	-	-
Guam	-	-	U	-	1	-	-	-	-
P.R.	170	110	-	29	92	-	1	-	8
V.I.	5	4	-	-	-	-	-	-	-
Pac. Trust Terr.	-	-	U	-	-	-	-	-	-

U: Unavailable

TABLE IV. Deaths in 121 U.S. cities,* week ending March 3, 1984 (9th Week Ending)

Reporting Area	All Causes, By Age (Years)						P&I** Total
	All Ages	≥65	45-64	25-44	1-24	<1	
NEW ENGLAND	699	498	151	25	10	15	67
Boston, Mass.	200	135	51	5	2	7	30
Bridgeport, Conn.	43	30	9	4	-	-	4
Cambridge, Mass.	32	24	4	4	-	-	4
Fall River, Mass.	29	21	7	-	-	1	-
Hartford, Conn.	58	42	12	1	2	1	2
Lowell, Mass.	32	23	7	-	-	2	5
Lynn, Mass.	18	16	2	-	-	-	2
New Bedford, Mass.	34	26	8	-	-	-	4
New Haven, Conn.	40	23	10	4	2	1	-
Providence, R.I.	67	46	17	2	1	1	5
Somerville, Mass.	12	9	3	-	-	-	-
Springfield, Mass.	46	34	7	3	2	-	4
Waterbury, Conn.	34	24	7	2	1	-	2
Worcester, Mass.	54	45	7	-	-	2	5
MID. ATLANTIC	2,764	1,871	593	187	55	57	128
Albany, N.Y.	51	34	15	2	-	-	2
Allentown, Pa.	23	19	4	-	-	-	-
Buffalo, N.Y.	105	64	27	9	1	4	10
Camden, N.J.	47	31	7	2	4	3	2
Elizabeth, N.J.	22	16	6	-	-	-	1
Erie, Pa.†	35	31	4	-	-	-	3
Jersey City, N.J.	58	41	6	6	2	3	1
N.Y. City, N.Y.	1,570	1,063	337	114	27	29	73
Newark, N.J.	75	40	18	7	6	4	2
Paterson, N.J.	27	15	8	3	-	1	2
Philadelphia, Pa.†	296	180	75	26	6	9	12
Pittsburgh, Pa.†	64	48	12	1	3	-	2
Reading, Pa.	25	20	3	2	-	-	-
Rochester, N.Y.	112	86	18	5	1	2	6
Schenectady, N.Y.	26	19	7	-	-	-	2
Scranton, Pa.†	30	24	4	2	-	-	2
Syracuse, N.Y.	92	63	22	3	4	-	2
Trenton, N.J.	38	22	11	3	1	1	1
Utica, N.Y.	28	21	7	-	-	-	-
Yonkers, N.Y.	40	34	2	2	-	1	5
E.N. CENTRAL	2,319	1,438	553	153	89	86	79
Akron, Ohio	65	35	17	4	6	3	-
Canton, Ohio	48	30	12	4	-	2	1
Chicago, Ill	556	328	133	45	21	29	15
Cincinnati, Ohio	166	101	44	11	6	4	14
Cleveland, Ohio	156	98	39	9	5	5	5
Columbus, Ohio	130	69	40	7	7	7	-
Dayton, Ohio	111	72	30	5	2	2	1
Detroit, Mich.	265	160	51	25	15	14	6
Evansville, Ind.	37	23	10	2	-	2	1
Fort Wayne, Ind.	50	31	15	2	1	1	2
Gary, Ind.	13	3	5	1	4	-	-
Grand Rapids, Mich.	73	47	18	4	2	2	3
Indianapolis, Ind.	153	85	43	12	9	4	6
Madison, Wis.	36	27	5	2	1	1	5
Milwaukee, Wis.	146	101	30	6	3	6	4
Peoria, Ill.	53	40	10	2	1	-	3
Rockford, Ill.	39	27	8	2	2	-	5
South Bend, Ind.	56	45	6	2	3	-	5
Toledo, Ohio	109	78	21	6	1	3	3
Youngstown, Ohio	57	38	16	2	-	1	-
W.N. CENTRAL	776	520	162	39	23	31	29
Des Moines, Iowa	37	27	7	2	-	1	3
Duluth, Minn.	34	23	7	1	-	3	-
Kansas City, Kans.	41	24	11	3	3	-	1
Kansas City, Mo.	111	73	28	3	4	2	6
Lincoln, Nebr.	16	12	-	-	2	2	-
Minneapolis, Minn.	105	70	15	7	5	8	1
Omaha, Nebr.	95	58	27	5	2	3	5
St. Louis, Mo.	180	123	40	9	4	4	7
St. Paul, Minn.	77	56	13	6	1	1	2
Wichita, Kans.	80	54	14	3	2	7	4
S. ATLANTIC	1,518	983	348	109	40	38	57
Atlanta, Ga.	152	91	43	14	3	1	5
Baltimore, Md.	428	252	115	35	16	10	11
Charlotte, N.C.	69	47	12	4	1	5	1
Jacksonville, Fla.	96	60	26	6	2	2	8
Miami, Fla.	132	87	29	10	1	5	1
Norfolk, Va.	61	33	17	3	4	4	5
Richmond, Va.	73	43	19	8	1	2	7
Savannah, Ga.	38	24	8	4	2	-	3
St. Petersburg, Fla.	131	116	11	1	1	2	6
Tampa, Fla.	82	54	18	5	1	4	2
Washington, D.C.	210	148	34	19	8	1	5
Wilmington, Del.	46	28	16	-	-	2	3
E.S. CENTRAL	872	549	213	55	16	39	42
Birmingham, Ala.	117	70	31	7	2	7	3
Chattanooga, Tenn.	78	48	22	3	1	4	3
Knoxville, Tenn.	62	41	14	3	1	3	-
Louisville, Ky.	105	63	33	6	2	1	7
Memphis, Tenn.	216	134	46	15	6	15	15
Mobile, Ala.	129	82	30	12	2	3	5
Montgomery, Ala.	35	23	8	3	-	1	1
Nashville, Tenn.	130	88	29	6	2	5	8
W.S. CENTRAL	1,605	963	381	129	64	67	90
Austin, Tex.	77	51	13	7	2	4	2
Baton Rouge, La.	42	26	8	3	5	-	-
Corpus Christi, Tex.	31	21	6	-	2	2	2
Dallas, Tex.	230	133	60	14	14	9	15
El Paso, Tex.	92	63	14	7	5	3	12
Fort Worth, Tex.	112	71	27	8	-	6	13
Houston, Tex.	398	203	109	53	15	18	16
Little Rock, Ark.	101	62	25	7	3	4	9
New Orleans, La.	149	97	30	7	5	10	-
San Antonio, Tex.	185	120	44	8	10	3	14
Shreveport, La.	65	39	18	6	1	1	-
Tulsa, Okla.	123	77	27	9	2	7	7
MOUNTAIN	707	452	150	57	20	28	41
Albuquerque, N.Mex.	68	42	15	7	2	2	6
Colo. Springs, Colo.	37	21	9	2	2	3	5
Denver, Colo.	151	97	32	9	4	9	5
Las Vegas, Nev.	80	49	19	5	4	3	5
Ogden, Utah	25	23	2	-	-	-	3
Phoenix, Ariz.	157	87	35	25	5	5	4
Pueblo, Colo.	28	26	2	-	-	-	2
Salt Lake City, Utah	63	40	12	4	3	4	2
Tucson, Ariz.	98	67	24	5	-	2	9
PACIFIC	1,905	1,325	358	125	27	67	124
Berkeley, Calif.	16	11	4	1	-	-	-
Fresno, Calif.	49	30	13	-	-	6	3
Glendale, Calif.	33	26	3	2	-	2	-
Honolulu, Hawaii	75	53	17	4	-	1	7
Long Beach, Calif.	106	80	16	7	1	2	23
Los Angeles, Calif.	404	296	66	29	5	8	1
Oakland, Calif.	79	45	22	9	1	2	5
Pasadena, Calif.	33	21	7	1	1	3	1
Portland, Oreg.	177	118	36	8	6	7	15
Sacramento, Calif.	57	44	7	5	-	1	6
San Diego, Calif.	177	117	39	12	3	6	22
San Francisco, Calif.	183	127	32	16	-	7	8
San Jose, Calif.	173	117	28	13	5	10	17
Seattle, Wash.	204	146	32	12	4	10	4
Spokane, Wash.	61	44	14	2	-	1	7
Tacoma, Wash.	78	50	22	4	1	1	5
TOTAL	13,165††	8,599	2,909	879	344	428	657

* 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 4 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.

Japanese Encephalitis — Continued

Reported by WHO Weekly Epidemiological Record *1984:59;21-2; Div of Vector-Borne Viral Diseases, Center for Infectious Diseases, CDC.*

Editorial Note: Under an investigational new drug (IND) permit issued by the U.S. Food and Drug Administration's Bureau of Biologics, CDC is sponsoring the evaluation of an inactivated, highly purified mouse brain JE vaccine manufactured by Biken Laboratories, Osaka, Japan. This vaccine has been administered to 88 participants according to the manufacturer's recommendation in two doses at an interval of 7-10 days. By testing for presence of neutralizing antibody in sera obtained before vaccination and about 21 days after the second dose, a seroconversion to a titer of 8 or higher occurred in 72% of 68 seronegative participants. Before recommending a wider use of this vaccine for selected persons traveling to JE-endemic areas, an evaluation of a three-dose schedule (at 7-day intervals) will be done in an effort to induce a more satisfactory neutralizing antibody response.

For this stage of the IND evaluation, about 100 participants are being recruited by collaborators in five U.S. locations. Candidates to receive the vaccine are selected primarily from among persons who plan to visit JE-endemic areas for 3 weeks or more during the season of principal JE activity (June to October in temperate climates) and whose itineraries include activities—such as travel to rural areas—with increased risk of exposure to mosquito vectors.

The risk of any traveler developing JE is low, and short-term visits and tours confined to urban centers further decrease this low risk. Whether or not the traveler is vaccinated, precautions to guard against mosquito bites should be taken. These include: minimizing outdoor exposure at dusk and dawn and on overcast days; sleeping in screened quarters or under mosquito netting; wearing clothing leaving a minimum of bare skin; and using insect repellents on exposed skin surfaces. Preferable repellents are those containing over 30% active ingredient (N, N-diethyl-meta-toluamide commonly abbreviated "DEET").

Until the experimental vaccine is more widely available in the United States, travelers who wish to be considered for vaccination should inquire about the availability of the vaccine at American Embassies in destination countries where JE is endemic.

Leading Work-Related Diseases and Injuries — United States

The National Institute for Occupational Safety and Health (NIOSH) has developed a suggested list of the 10 leading work-related diseases and injuries (1). *The first two categories, "Occupational Lung Diseases" and "Musculoskeletal Injuries," were recently described* (1,2); *a discussion of the third category, "Occupational Cancers (Other than Lung)," appears below.*

OCCUPATIONAL CANCERS (OTHER THAN LUNG)

Cancer kills approximately 430,000 people in the United States annually; the American Cancer Society estimates that some form of cancer will develop in one-fourth of all Americans (*3*). It is the second leading cause of death and the second leading cause of lost years of potential life in this country (*4*). A high proportion of all cancers are thought to be caused by "extragenetic" factors, including behaviors (e.g., cigarette smoking, alcohol and drug use, and sexual activities) and toxic environmental exposures in the workplace and the community (*5*). Evidence for these relationships has been developed principally through epidemiologic and toxicologic studies. The main epidemiologic observations have included: differences in the incidence of cancer between groups with different exposures, changes in the incidence of cancer following migrations, changes in the incidence of cancer over time, etc. Toxicologic studies have led to the identification of specific agents that cause cancer in experimental animals (*5*).

A possible occupational origin for malignant disease was first recognized when an unusually high frequency of scrotal cancer was observed among London chimney sweeps in 1775 (*6*).

Work-Related Diseases and Injuries — Continued

Since then, several types of cancer have been associated with industrial agents or processes (Table 1) (*7*). Numerous other occupational agents—such as beryllium, cadmium, ethylene oxide, phenoxy-acetic acids, and chlorophenols—or processes—such as newsprint pressroom work—are suspected of being carcinogenic and are under investigation by NIOSH.

Although general agreement exists concerning the overall incidence of cancer, considerable controversy surrounds the proportion of cancer cases attributable to occupational exposures. Several characteristics of cancer contribute to the difficulty in making such estimates:

1. Latency in the development of cancer. Occupational cancer usually becomes evident long after initial exposure to the carcinogen; this interval may vary from 5 years to more than 40 years (*9*), making it difficult to characterize important exposures long past.
2. Influence of exposures to multiple carcinogens. Cancer victims may have been occupationally exposed to many carcinogens; interaction of these agents or interactions between them and other factors may greatly increase the risk of cancer (*10*).

Table 1. Selected occupational cancers*

ICD-9†	Condition	Industry/occupation	Agent
155	Hemangiosarcoma of the liver	Vinyl chloride polymerization Industry vintners	Vinyl chloride monomer Arsenical pesticides
160.0	Malignant neoplasm of nasal cavities	Woodworkers, cabinet/furniture makers Boot and shoe producers Radium chemists, processors, dial painters Nickel smelting and refining	Hardwood dusts Unknown Radium Nickel
161	Malignant neoplasm of larynx	Asbestos industries and utilizers	Asbestos
158, 163	Mesothelioma (peritoneum) (pleura)	Asbestos industries and utilizers	Asbestos
170	Malignant neoplasm of bone	Radium chemists, processors, dial painters	Radium
187.7	Malignant neoplasm of scrotum	Automatic lathe operators, metalworkers Coke oven workers, petroleum refiners, tar distillers	Mineral/cutting oils Soots and tars, tar distillates
188	Malignant neoplasm of bladder	Rubber and dye workers	Benzidine, alpha and beta naphthylamine, auramine, magenta, 4-aminobiphenyl, 4-nitrophenyl
189	Malignant neoplasm of kidney; other, and unspecified urinary organs	Coke oven workers	Coke oven emissions
204	Lymphoid leukemia, acute	Rubber industry Radiologists	Unknown Ionizing radiation
205	Myeloid leukemia, acute	Occupations with exposure to benzene Radiologists	Benzene Ionizing radiation
207.0	Erythroleukemia	Occupations with exposure to benzene	Benzene

*Adapted from reference *7*.

†Modified International Classification of Diseases (ICD) rubric.

Work-Related Diseases and Injuries – Continued

3. Influence of behavioral factors. Cigarette smoking, alcohol drinking, and dietary habits also influence the development of cancer (*11*). Moreover, these factors—especially cigarette smoking—interact with chemical and physical agents in the working environment to increase the risk of cancer (*12*); e.g., exposure to asbestos interacts with cigarette smoking to greatly increase the risk of lung cancer.

In addition, problems with the documentation of cancer and the nature and extent of etiologic exposures obscure important epidemiologic associations:

1. Errors in diagnosis and classification of cancer. Unusual neoplasms are often misdiagnosed; even correct diagnoses may be improperly categorized according to the International Classification of Diseases (ICD); an example is mesothelioma (*10*).
2. Lack of meaningful occupational histories. In only a few states is information collected on the work histories of cancer victims; hence, for many cases, crucial associations with occupational carcinogens are not apparent.
3. Difficulty in assessing exposures quantitatively. Precise measurements of levels and duration of exposures have not generally been available (*13*). Consequently, the ability to delineate dose-response relationships has been very limited.
4. The frequency of specific types of cancers. The occupational etiology of a very rare cancer due to a specific agent (e.g., hemangiosarcoma of the liver due to vinyl chloride) is much more readily documented than the occupational etiology of a cancer type potentially caused by several factors (e.g., lung cancer associated with exposure to chromates).
5. The "dilution factor." Highly significant differences in the rates of cancer among small subgroups of a population may be overlooked because these rates affect the overall rate for cancer in the larger study population only slightly, if at all (*8*).

Despite these difficulties, various attempts have been made to estimate the proportion of cancers related to occupation. These estimates span a broad range, from less than 4% (*5,14*) to more than 20% (*15*). While these estimates are obviously imprecise, little doubt remains that occupational factors are significantly related to an increased risk of cancer. Moreover, in specific groups of workers exposed to specific carcinogens, the proportion who ultimately develop occupational cancer may be large. Of one group of workers distilling beta-naphthylamine who had more than 5 years of exposure, all reportedly developed tumors of the bladder (*17*); up to 11% of workers exposed to asbestos may ultimately develop mesothelial tumors (*16*).

Reported by Div of Surveillance, Hazard Evaluations, and Field Studies, NIOSH, CDC.

Editorial Note: Cancer caused by occupational agents, especially synthetic chemicals, is a problem of human origin, and should, therefore, be preventable. Substitution of noncarcinogens for carcinogens, enforcement of protective standards for exposure, design and application of engineering controls, and use of personal protective equipment by exposed workers are major modes of prevention.

Although it is difficult to predict a trend for the future incidence of occupational cancer, the increased volume and diversity of synthetic chemicals manufactured since World War II (*18*) raise serious concern about the risks from exposure to these substances. However, improved control technology, governmental regulatory activity to reduce exposures, surveillance of disease and risk factors, and vigilant use of preventive measures will ultimately reduce occupational cancer.

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*Additional references are available on request from the National Institute for Occupational Safety and Health, CDC.

Work-Related Diseases and Injuries — Continued

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