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Epidemiologic Notes and Reports

Systemic Allergic Reactions Following Immunization with Human Diploid Cell Rabies Vaccine

Human diploid cell rabies vaccine (HDCV) has been licensed for use since June 9, 1980. Approximately 400,000 doses have been administered to an estimated 100,000 persons in the United States since that time. The majority of these were for postexposure treatments. Information on possible adverse reactions to HDCV has been collected by CDC from individual physicians and from medical personnel in charge of providing rabies preexposure and postexposure prophylaxis to large cohorts of persons, such as veterinary students and animal-control workers. During the past 46 months, 108 clinical reports of systemic allergic reactions ranging from hives to anaphylaxis were reported to CDC (11 per 10,000 vaccinees). Few patients required hospitalization, and no deaths secondary to the reactions were reported.

The reports of systemic allergic reactions included nine cases of presumed Type I immediate hypersensitivity (1/10,000), 87 cases of presumed Type III hypersensitivity reactions (9/10,000), and 12 cases of allergic reactions of indeterminate type (Table 1). These reactions were classified on the basis of clinical observations only. Type I hypersensitivity reactions refer to immunoglobulin E (IgE)-mediated immediate reactions, such as anaphylaxis and atopy, whereas Type III hypersensitivity refers to immunoglobulin G (IgG)- or immunoglobulin M (IgM)-mediated immune complex disease characterized by antigen-antibody complex deposition in tissues, complement activation, and inflammation (*1*).

Hypersensitivity reactions presumed to be Type III occurred 2-21 days after a dose or doses of HDCV; patients presented with a generalized or pruritic rash or urticaria, sometimes accompanied by arthralgias, angioedema, fever, nausea, vomiting, and malaise. All nine of the presumed immediate hypersensitivity reactions occurred during either primary preexposure immunization (vaccine administered on days 0, 7, and 21 *or* 28) or postexposure immunization (vaccine on days 0, 3, 7, 14, and 28 and rabies immune globulin on day 0). However, 81 (93%) of 87 of the presumed Type III hypersensitivity reactions were observed following booster immunization. Although the presumed Type III reactions occurred in six persons during primary immunization series, none were observed following the first dose of the primary series.

Routine boosters of HDCV at 2-year intervals have been recommended for persons with continuing risks of exposure. As increasing numbers of persons received their first routine 2-year boosters, reports of presumed Type III hypersensitivity reactions increased in frequency. In approximately half of known cohorts who received booster immunizations between January 1982 and March 1984, some recipients had presumed Type III hypersensitivity reactions. Sixty-seven (7%) of 962 persons in these cohorts fit the above case description for presumed Type III hypersensivity reactions.

Human Diploid Cell Rabies Vaccine — Continued

Table 2 illustrates the clinical features in three of the cohorts reporting presumed Type III reactions following booster immunization with HDCV. When performed, urinalyses, blood urea nitrogen (BUN), and serum creatinine determinations have been normal. Elevated white blood cell counts ranging from 14,000 to 24,000 (predominantly polymorphonuclear leukocytes) were reported in two cases. Serum complement levels (C-3, C-4, and CH-50) were depressed in two patients when serum was drawn at the time of most active clinical symptoms; one of these also had detectable cryoglobulins. Serum-complement levels were normal in five other patients whose sera were collected at other times. Respiratory distress was infrequently seen. Most patients' symptoms improved within 2-3 days when treated with antihistamines, but a few required systemic corticosteroids and epinephrine.

Preliminary analysis of epidemiologic features of the illness in several cohorts revealed a male/female relative risk of 2.3 (95% confidence limits, 1.2-4.4). No significant associations have been demonstrated between persons who reported presumed Type III hypersensitivity reactions and age, route of primary or booster immunization (intramuscular or intradermal), timing of booster after primary immunization, history of other allergies, or history of previous immunization with rabies vaccines other than HDCV. HDCV produced by both Merieux Institute and Wyeth Laboratories has been associated with reactions. In two groups for which serologic data were available, no difference was shown in pre-booster antibody titers between reactors and nonreactors, but post-booster titers were significantly higher in those who developed reactions. Most presumed Type III reactions were reported to have occurred following booster doses, but six occurred following two or more doses of HDCV given for primary immunization.

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Table 1. Reports of systemic allergic reactions following immunization with human diploid cell rabies vaccine — United States, June 1980-March 1984

	Preexposure				Postexposure		
	Primary series		Booster dose		Primary series	Booster dose	Total
Reaction type*	ID†	IM§	ID	IM	IM	IM	
Type I (immediate hypersensitivity)	1	0	0	0	8	0	9
Type III (immune complex disease)	1	0	42	34	5	5	87
Indeterminate (Type I or Type III)	0	0	0	0	11	1	12
Total	2	0	42	34	24	6	108

*Characterization of reactions is based on clinical definition, not immunopathologic changes:

Type I: Immediate hypersensitivity, as used here, refers to an immunologic illness occurring within minutes to hours after a dose of HDCV and characterized with either bronchospasm, laryngeal edema, generalized pruritic rash, urticaria, or angioedema.

Type III: Presumed immune complex disease, as used here, refers to an immunologic illness occurring 2-21 days after a dose or doses of HDCV and characterized by a generalized pruritic rash or urticaria; the patient may also have arthralgias, arthritis, angioedema, nausea, vomiting, fever, and malaise.

†Intradermal.

§Intramuscular.

Human Diploid Cell Rabies Vaccine – Continued

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Editorial Note: Primary immunization with HDCV appears to sensitize some recipients to an, as yet, unidentified component of the vaccine. When booster doses of HDCV are then administered, these persons develop a hypersensitivity reaction clinically consistent with Type III immune complex disease. Until this reaction problem can be resolved, it would be prudent to carefully assess each use of rabies vaccine for routine booster immunization. Persons who have experienced Type III hypersensivity reactions should receive no further doses of HDCV unless: (1) they are exposed to rabies* or (2) they are truly likely to be inapparently and/or unavoidably exposed to rabies virus and have unsatisfactory antibody titers. The routine use of booster immunization in persons without histories of hypersensivity reactions is clearly indicated only in those subjected to inapparent and/or unavoidable exposures to rabies virus. All available data suggest an anamnestic antibody response will occur in any person who previously received primary preexposure immunization with HDCV, even when the antibody titer at the time of the booster was low or undetectable.

Individuals with histories of presumed Type III hypersensitivity to HDCV may be at higher risk of subsequent hypersensitivity reactions, and vaccine should be administered under appropriate medical supervision.

References

1. Coombs RRA, Gell PGH. Classification of allergic reactions responsible for clinical hypersensitivity and disease. In: Gell PGH, Coombs RRA, Lachmann PJ, eds. Clinical aspects of immunology. 3rd ed. Oxford: Blackwell Scientific Publications, 1975:761-81.

*Postexposure prophylaxis in previously immunized persons consists of two 1-ml intramuscular doses of HDCV, one each on days 0 and 3.

Table 2. Signs and symptoms in three cohorts reporting presumed immune complex-type hypersensitivity reactions* after booster immunization with human diploid cell rabies vaccine

	Cohort A	Cohort B	Cohort C
No. with reaction/total persons given boosters (%)	23/226 (10%)	22/123 (18%)	6/29 (21%)
Vaccine	Merieux	Wyeth	Merieux
Route of booster	ID†	IM§	IM
No. with sign or symptom (%)¶:			
Pruritic rash	16 (70%)	5 (18%)	1 (17%)
Urticaria	20 (87%)	20 (91%)	6 (100%)
Edema	10 (43%)	10 (45%)	4 (67%)
Joint pain	4 (17%)	3 (14%)	0
Fever	1 (4%)	0	0
Difficulty breathing	1 (4%)	2 (9%)	0
Mean delay after booster before reaction (range)	9.4 days (3-13)	8.6 days (2-11)	10.5 days (8-11)

*Coombs and Gell Type III.
†Intradermal.
§Intramuscular.
¶Total in each cohort greater than 100%, because multiple signs and symptoms could be reported in each person.

Current Trends

Rocky Mountain Spotted Fever — United States, 1983

For 1983, a provisional total of 1,126 cases of Rocky Mountain spotted fever (RMSF) in the United States was reported to CDC, for an incidence rate of 0.5 cases/100,000 population.

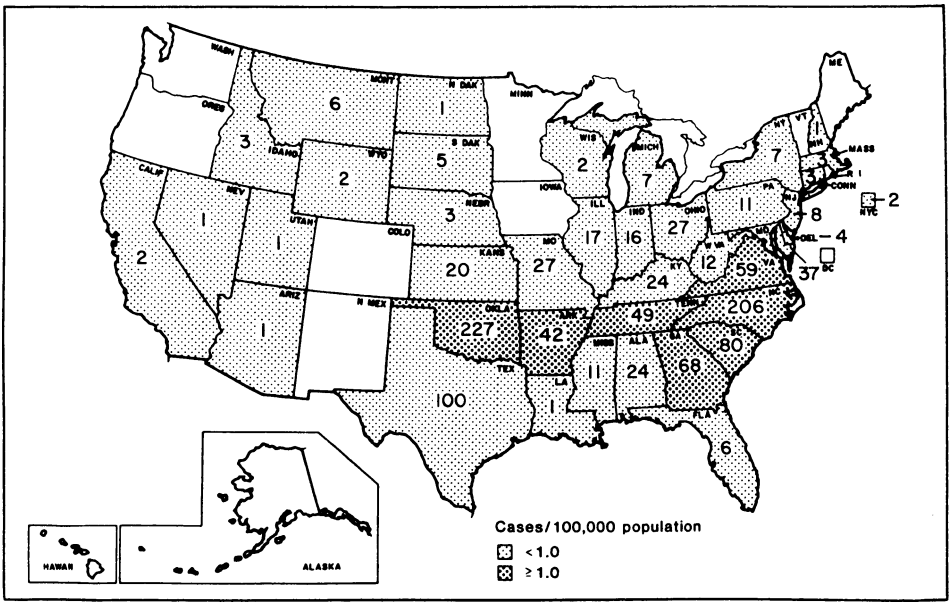
Oklahoma reported the most cases and had the highest incidence rate in the country (227 cases, 6.9/100,000 population). Other states with high RMSF rates were: North Carolina (206 cases, 3.4/100,000); South Carolina (80 cases, 2.5/100,000); Arkansas (42 cases, 1.8/100,000); Georgia (68 cases, 1.2/100,000); Virginia (59 cases, 1.1/100,000); and Tennessee (49 cases, 1.1/100,000) (Figure 1).

States submitted case report forms for 957 (85%) of reported cases. Of these, 603 (63%) were confirmed by serologic testing,* by isolation of spotted fever group rickettsiae, or by fluorescent antibody staining of biopsy or autopsy specimens. An additional 60 patients (6%) had "probable" cases, as indicated by a fourfold increase or a single convalescent titer 1:320 or higher in the Weil-Felix (OX-19, OX-2) agglutination tests, or by a single convalescent titer 1:128 or higher by latex agglutination (LA) or indirect hemagglutination (IHA). The other 294 cases (31%) were reported on the basis of clinical diagnoses alone. Fifty-one percent of the patients were under 20 years of age; 61% were male; and 89% were white.

Ninety-four percent of patients became ill between April 1 and September 30. Symptoms reported included fever (97%), headache (87%), rash on torso (85%), and rash on palms of hands or soles of feet (62%). Seventy-seven percent of patients were hospitalized. Sixty-seven percent of patients for whom exposure information was available reported tick bites or

*A fourfold increase in antibody titer between acute- and convalescent-phase serum specimens by complement fixation (CF), indirect fluorescent antibody (IFA), indirect hemagglutination, latex agglutination, or microagglutination; or a single convalescent titer 1:16 or higher (CF) or 1:64 or higher (IFA) in a clinically compatible case.

FIGURE 1. Reported cases of Rocky Mountain spotted fever, by state — United States, 1983



Rocky Mountain Spotted Fever – Continued

attachments within 14 days before onset of illness. The case-fatality rate (4%) was higher for persons 30 years of age or older (9%) than for younger individuals (2%); slightly higher for persons with unknown or no tick exposure (5%) than for persons reporting tick bites or attachments (4%); and higher for persons not reporting treatment with tetracycline or chloramphenicol (7%) than for those who received such antibiotic therapy (4%).

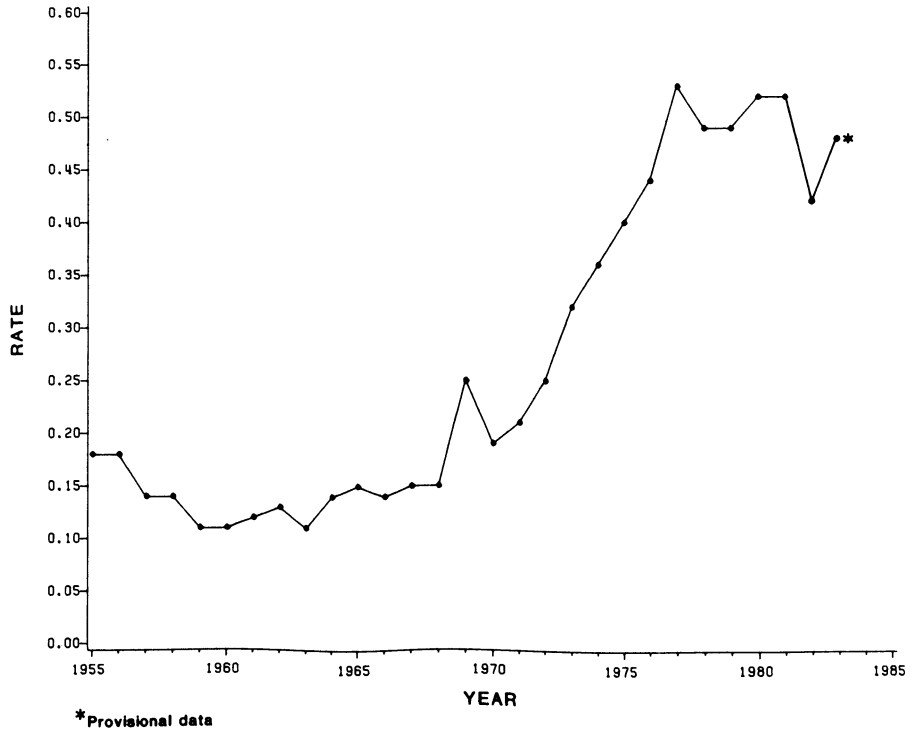
Nineteen percent of 666 patients for whom histories were available reported travel outside their counties of residence within 14 days before onset of illness. Forty-six percent of these patients indicated travel to one of the seven states reporting the highest incidence of RMSF in 1983.

Reported by Div of Viral Diseases, Center for Infectious Diseases, CDC.

Editorial Note: After the rapid rise of RMSF in the United States during the 1970s, infection rates have remained approximately the same since 1977, with the exception of a slight drop in 1982 (Figure 2). In 1983, more cases than usual were reported from Oklahoma, Arkansas, and Texas (Texas reported 100 cases, for an incidence of 0.6/100,000), suggesting increased activity of RMSF in the West South Central states, where the vectors of RMSF are *Amblyomma americanum* (the Lone-Star tick) and *Dermacentor variabilis* (the American dog tick). Four hundred seventy-two cases (42% of the total) were reported from the South Atlantic states, where the principal vector is *D. variabilis*.

The higher incidence of RMSF among younger persons and the case-fatality rate (which has fluctuated between 3% and 8% since 1970) have changed little in recent years. Consistent with previous findings (*1*), the 1983 data indicate that fatality continues to be associated with persons aged 30 years or older, failure to obtain a history of exposure to ticks, and lack

FIGURE 2. Reported cases of Rocky Mountain spotted fever per 100,000 population, by year — United States, 1955-1983



*Provisional data

Rocky Mountain Spotted Fever – Continued

of appropriate antibiotic therapy. Travel history for 19% of patients for whom information was available indicates that travel to highly endemic areas may be critical in diagnosing the disease, especially in areas where RMSF does not commonly occur.

The percentage of laboratory-confirmed (63%) cases in 1983 was higher than that in 1982 (48%) and 1981 (35%), suggesting that the more sensitive and specific laboratory tests to confirm RMSF have achieved wider use. It must be emphasized, however, that RMSF confirmation is of epidemiologic importance and cannot usually be expected to occur before 10-14 days after onset of illness. Therefore, diagnosis must rely on clinical (fever, headache, rash, myalgia) and epidemiologic (tick exposure) criteria, and treatment with tetracycline or chloramphenicol must be initiated before laboratory confirmation is available.

Prevention of RMSF entails frequent inspection of persons when tick exposure is likely. Ticks are best removed by grasping with tweezers as close as possible to the point of attachment and by pulling slowly and steadily. If tweezers are unavailable, fingers protected with facial tissue may be used. If bare hands touch the tick during removal, the hands should be washed thoroughly with soap and water, because ticks' secretions can be infective. Because it is difficult to determine with certainty if a tick is infected with *Rickettsia rickettsii*, or if transmission has occurred, routine testing of ticks removed from patients is not recommended.

(Continued on page 195)

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

Disease	14th Week Ending			Cumulative, 14th Week Ending		
	April 7, 1984	April 9, 1983	Median 1979-1983	April 7, 1984	April 9, 1983	Median 1979-1983
Acquired Immunodeficiency Syndrome (AIDS)	68	N	N	948	N	N
Aseptic meningitis	72	74	58	1,079	1,121	912
Encephalitis: Primary (arthropod-borne & unspec.)	18	17	13	206	255	221
Post-infectious	2	1	4	12	21	24
Gonorrhea: Civilian	14,050	15,877	18,068	215,216	241,253	252,498
Military	414	471	547	5,471	6,485	7,330
Hepatitis: Type A	344	390	530	5,966	6,509	6,799
Type B	450	433	391	6,141	5,865	5,060
Non A, Non B	84	64	N	889	862	N
Unspecified	66	153	191	1,590	2,024	2,748
Legionellosis	7	7	N	131	152	N
Leprosy	3	3	3	50	66	52
Malaria	10	20	20	149	178	201
Measles: Total*	50	47	79	488	544	752
Indigenous	46	44	N	448	475	N
Imported	4	3	N	40	69	N
Meningococcal infections: Total	74	89	84	937	926	958
Civilian	74	89	84	937	914	949
Military	-	-	-	-	12	9
Mumps	64	58	270	982	1,145	2,069
Pertussis	34	68	20	459	422	288
Rubella (German measles)	14	25	78	148	308	738
Syphilis (Primary & Secondary): Civilian	446	609	608	7,576	8,958	8,159
Military	4	3	3	89	129	100
Toxic Shock syndrome	15	10	N	94	127	N
Tuberculosis	451	428	509	5,377	5,723	6,530
Tularemia	2	4	3	21	40	27
Typhoid fever	2	9	5	69	96	108
Typhus fever, tick-borne (RMSF)	2	3	2	15	18	17
Rabies, animal	89	200	141	1,163	1,649	1,424

TABLE II. Notifiable diseases of low frequency, United States

	Cum. 1984		Cum. 1984
Anthrax	-	Plague	2
Botulism: Foodborne	4	Poliomyelitis: Total	-
Infant (Tenn. 1, Wyo. 1, Calif. 3)	29	Paralytic	-
Other	2	Psittacosis	17
Brucellosis (Ga. 1, Okla. 1)	27	Rabies, human	-
Cholera	-	Tetanus (Iowa 1)	8
Congenital rubella syndrome	1	Trichinosis	8
Diphtheria	-	Typhus fever, flea-borne (endemic, murine)	6
Leptospirosis	5		

*Two of the 50 reported cases for this week were 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 April 7, 1984 and April 9, 1983 (14th 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	948	72	206	12	215,216	241,253	344	450	84	66	7	50
NEW ENGLAND	33	4	15	-	6,763	6,032	9	27	2	10	-	2
Maine	-	-	-	-	258	345	2	-	-	-	-	-
N.H.	1	-	4	-	164	178	1	3	-	-	-	-
Vt.	-	-	2	-	102	96	1	1	-	-	-	-
Mass.	20	1	6	-	2,637	2,730	2	9	-	9	-	2
R.I.	-	3	-	-	402	327	3	9	-	-	-	-
Conn.	12	-	3	-	3,200	2,356	-	5	2	1	-	-
MID ATLANTIC	443	7	25	-	30,158	30,914	66	59	8	5	-	2
Upstate N.Y.	41	-	5	-	4,554	4,473	9	17	4	2	-	2
N.Y. City	326	5	-	-	13,283	13,145	33	20	-	2	-	-
N.J.	65	-	13	-	4,740	5,695	24	22	4	1	-	-
Pa.	11	2	7	-	7,581	7,601	U	U	U	U	-	-
E.N. CENTRAL	43	14	45	4	26,762	33,899	17	41	7	2	2	3
Ohio	9	12	16	2	7,310	8,409	7	11	3	-	1	1
Ind.	7	1	9	-	3,354	3,849	1	4	-	1	-	-
Ill.	21	-	7	2	4,380	9,262	2	-	-	-	1	-
Mich.	4	1	10	-	8,302	9,403	7	26	4	1	-	2
Wis.	2	-	3	-	3,416	2,976	-	-	-	-	-	-
W.N. CENTRAL	6	2	4	-	10,160	11,397	16	15	4	-	1	-
Minn.	1	-	-	-	1,449	1,654	3	1	-	-	-	-
Iowa	-	1	3	-	1,185	1,202	1	2	1	-	-	-
Mo.	3	1	-	-	4,684	5,568	4	3	3	-	-	-
N. Dak.	-	-	-	-	111	111	-	-	-	-	-	-
S. Dak.	-	-	-	-	301	336	4	1	-	-	-	-
Nebr.	1	-	-	-	735	610	2	5	-	-	-	-
Kans.	1	-	1	-	1,695	1,916	2	3	-	-	1	-
S. ATLANTIC	118	15	39	5	55,365	62,727	28	104	22	10	1	2
Del.	3	-	1	-	926	1,138	1	-	-	-	-	-
Md.	13	2	9	-	6,828	7,822	2	15	4	-	-	-
D.C.	14	-	-	-	4,030	4,294	-	1	-	-	-	-
Va.	7	-	11	3	5,357	5,228	3	10	2	-	-	1
W. Va.	1	-	3	-	653	592	-	-	-	-	-	-
N.C.	2	2	7	1	8,897	8,614	-	11	2	3	-	-
S.C.	3	-	1	-	5,192	5,958	-	19	-	1	-	-
Ga.	13	2	3	-	10,708	14,390	3	9	4	1	-	-
Fla.	62	9	4	1	12,774	14,691	19	39	10	5	1	1
E.S. CENTRAL	6	9	10	-	18,416	20,628	7	35	4	4	-	-
Ky.	4	1	1	-	2,305	2,528	1	-	1	1	-	-
Tenn.	-	-	2	-	7,431	8,130	-	23	-	2	-	-
Ala.	1	8	7	-	5,933	6,430	2	10	3	1	-	-
Miss.	1	-	-	-	2,747	3,540	4	2	-	-	-	-
W.S. CENTRAL	41	-	14	1	29,288	33,141	15	10	-	9	-	3
Ark.	-	-	-	1	2,498	2,655	1	1	-	4	-	-
La.	8	-	2	-	6,301	4,858	8	7	-	-	-	-
Okla.	2	-	1	-	3,303	4,059	6	2	-	5	-	-
Tex.	31	-	11	-	17,186	21,569	-	-	-	-	-	3
MOUNTAIN	9	3	6	-	6,732	7,161	40	30	6	2	1	6
Mont.	-	-	-	-	310	344	-	-	1	-	-	-
Idaho	-	-	-	-	315	360	1	4	-	-	1	-
Wyo.	-	-	-	-	200	206	1	1	1	-	-	-
Colo.	4	1	3	-	1,925	2,083	16	8	2	-	-	-
N. Mex.	-	-	-	-	795	936	2	2	-	-	-	-
Ariz.	5	2	1	-	1,717	1,765	15	9	2	2	-	4
Utah	-	-	2	-	361	337	2	-	-	-	-	1
Nev.	-	-	-	-	1,109	1,130	3	6	-	-	-	1
PACIFIC	249	18	48	2	31,572	35,354	146	129	31	24	2	32
Wash.	8	1	1	-	2,106	2,667	3	4	6	-	-	2
Oreg.	1	-	-	-	1,850	1,792	10	10	1	2	-	1
Calif.	238	16	45	2	26,301	29,382	133	115	24	22	2	21
Alaska	-	-	-	-	771	796	-	-	-	-	-	-
Hawaii	2	1	2	-	544	717	-	-	-	-	-	8
Guam	-	U	-	-	50	56	U	U	U	U	U	-
P.R.	11	3	-	-	926	782	5	23	-	8	-	-
V.I.	-	-	-	-	112	79	-	-	-	-	-	-
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 April 7, 1984 and April 9, 1983 (14th 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	149	46	448	4	40	544	937	64	982	34	459	422	14	148	308
NEW ENGLAND	15	-	-	-	-	2	67	2	37	-	9	17	5	19	4
Maine	-	-	-	-	-	-	1	-	12	-	-	-	-	1	-
N.H.	-	-	-	-	-	-	4	1	5	-	2	3	-	-	2
Vt.	1	-	-	-	-	-	19	-	2	-	5	3	-	-	1
Mass.	8	-	-	-	-	1	21	-	12	-	1	10	5	18	1
R.I.	1	-	-	-	-	-	6	1	2	-	1	1	-	-	-
Conn.	5	-	-	-	-	1	16	-	4	-	-	-	-	-	-
MID ATLANTIC	16	3	15	2§	8	11	126	14	135	2	26	102	2	6	17
Upstate N.Y.	4	2	2	2§	2	2	47	1	30	2	16	37	2	4	11
N.Y. City	3	1	11	-	-	8	12	1	4	-	1	8	-	1	2
N.J.	6	-	-	-	3	1	33	12	92	-	1	8	-	1	1
Pa.	3	-	2	-	3	-	34	-	9	-	8	49	-	-	3
E.N. CENTRAL	17	14	128	-	2	317	150	20	349	21	174	113	1	18	49
Ohio	4	-	1	-	2	1	50	6	114	2	30	32	1	2	1
Ind.	-	-	3	-	-	217	19	1	22	17	115	7	-	1	2
Ill.	5	14	35	-	-	94	40	9	83	2	11	60	-	9	23
Mich.	4	-	89	-	-	5	28	4	105	-	10	6	-	4	9
Wis.	4	-	-	-	-	-	13	-	25	-	8	8	-	2	14
W.N. CENTRAL	6	-	-	-	-	-	53	2	64	-	62	24	1	16	19
Minn.	-	-	-	-	-	-	7	-	1	-	3	9	-	1	3
Iowa	1	-	-	-	-	-	13	1	14	-	3	2	-	-	-
Mo.	4	-	-	-	-	-	17	-	5	-	10	3	-	-	-
N. Dak.	-	-	-	-	-	-	1	-	1	-	-	1	1	3	-
S. Dak.	-	-	-	-	-	-	2	-	-	-	1	-	-	-	-
Nebr.	-	-	-	-	-	-	3	-	1	-	2	-	-	-	-
Kans.	1	-	-	-	-	-	10	1	42	-	43	9	-	12	16
S. ATLANTIC	23	-	1	-	5	107	224	6	81	1	48	59	-	14	30
Del.	2	-	-	-	-	-	1	-	2	-	-	-	-	-	-
Md.	6	-	-	-	-	2	18	-	17	-	3	12	-	-	-
D.C.	-	-	-	-	-	-	2	-	-	-	-	-	-	-	-
Va.	4	-	1	-	1	2	29	-	5	-	7	18	-	-	1
W. Va.	-	-	-	-	-	-	3	2	17	-	5	2	-	-	-
N.C.	3	-	-	-	-	-	27	-	10	-	17	2	-	-	4
S.C.	1	-	-	-	-	3	18	-	1	-	1	2	-	-	-
Ga.	1	-	-	-	-	6	49	3	8	-	2	17	-	2	5
Fla.	6	-	-	-	4	94	77	1	21	1	13	6	-	12	20
E.S. CENTRAL	1	-	1	-	2	-	37	2	17	-	2	5	-	1	5
Ky.	-	-	1	-	-	-	4	1	4	-	1	2	-	-	5
Tenn.	-	-	-	-	2	-	17	1	7	-	1	2	-	-	-
Ala.	1	-	-	-	-	-	11	-	3	-	-	-	-	1	-
Miss.	-	-	-	-	-	-	5	-	3	-	-	1	-	-	-
W.S. CENTRAL	6	5	94	-	5	42	112	1	52	1	41	31	-	12	51
Ark.	-	-	-	-	-	10	13	1	4	-	10	2	-	2	-
La.	1	-	-	-	-	-	22	-	-	1	2	2	-	-	9
Okla.	2	5	5	-	-	-	14	N	N	-	28	11	-	-	-
Tex.	3	-	89	-	5	32	63	-	48	-	1	16	-	10	42
MOUNTAIN	5	-	48	-	8	1	37	3	79	2	45	56	-	3	12
Mont.	-	-	-	-	-	-	1	-	3	-	19	1	-	-	3
Idaho	-	-	-	-	-	-	4	-	5	-	1	2	-	1	2
Wyo.	-	-	-	-	-	-	1	-	1	-	3	4	-	-	1
Colo.	1	-	-	-	-	1	15	-	8	-	12	34	-	-	-
N. Mex.	-	-	25	-	8	-	6	N	N	1	3	4	-	-	-
Ariz.	2	-	-	-	-	-	7	3	57	1	4	6	-	-	4
Utah	2	-	23	-	-	-	3	-	4	-	1	5	-	2	1
Nev.	-	-	-	-	-	-	-	-	1	-	2	-	-	-	1
PACIFIC	60	24	161	2	10	64	131	14	168	7	52	15	5	59	121
Wash.	3	11	39	-	-	1	20	-	21	-	8	1	-	1	1
Oreg.	1	-	-	-	-	5	19	N	N	1	6	2	-	-	8
Calif.	53	13	122	2†	8	57	89	14	138	3	22	12	5	57	112
Alaska	-	-	-	-	-	-	2	-	3	-	-	-	-	-	-
Hawaii	3	-	-	-	2	1	1	-	6	3	16	-	-	1	-
Guam	-	U	27	U	1	-	1	U	3	U	-	-	U	1	-
P.R.	2	-	-	-	-	47	3	1	40	-	-	3	-	1	1
V.I.	-	-	-	-	-	5	-	-	3	-	-	-	-	-	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 April 7, 1984 and April 9, 1983 (14th 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	7,576	8,958	15	5,377	5,723	21	69	15	1,163
NEW ENGLAND	172	219	-	142	151	1	1	-	6
Maine	1	4	-	8	11	-	-	-	6
N.H.	3	9	-	9	14	-	-	-	-
Vt.	-	1	-	3	1	-	-	-	-
Mass.	107	144	-	72	74	1	-	-	-
R.I.	7	6	-	14	16	-	-	-	-
Conn.	54	55	-	36	35	-	1	-	-
MID ATLANTIC	1,021	1,075	1	1,009	1,078	-	10	1	77
Upstate N.Y.	69	83	-	161	174	-	5	1	3
N.Y. City	615	643	-	417	421	-	2	-	-
N.J.	187	198	-	204	232	-	3	-	-
Pa.	150	151	1	227	251	-	-	-	74
E.N. CENTRAL	280	514	1	739	760	-	9	1	44
Ohio	60	128	1	142	129	-	3	1	3
Ind.	41	46	-	74	90	-	1	-	6
Ill.	60	245	-	306	320	-	2	-	26
Mich.	93	71	-	178	182	-	1	-	1
Wis.	26	24	-	39	39	-	2	-	8
W.N. CENTRAL	127	105	4	136	206	6	2	2	168
Minn.	27	47	1	22	34	-	2	-	17
Iowa	10	4	3	22	29	-	-	-	40
Mo.	71	37	-	63	106	6	-	2	14
N. Dak.	-	-	-	4	-	-	-	-	27
S. Dak.	2	-	-	3	16	-	-	-	45
Nebr.	6	5	-	7	5	-	-	-	9
Kans.	11	12	-	15	16	-	-	-	16
S. ATLANTIC	2,343	2,314	-	1,204	1,100	2	9	2	380
Del.	8	12	-	14	6	-	-	-	-
Md.	150	131	-	133	79	-	-	-	217
D.C.	85	96	-	41	40	-	3	-	-
Va.	119	169	-	113	96	-	3	1	87
W. Va.	8	6	-	49	48	-	-	-	10
N.C.	258	211	-	191	115	-	1	-	1
S.C.	218	161	-	128	101	-	1	1	8
Ga.	390	430	-	169	232	2	-	-	40
Fla.	1,107	1,098	-	366	383	-	1	-	17
E.S. CENTRAL	487	596	1	487	555	-	2	3	68
Ky.	26	35	-	117	146	-	-	-	16
Tenn.	118	155	-	157	163	-	2	1	33
Ala.	162	249	1	171	153	-	-	2	19
Miss.	181	157	-	42	93	-	-	-	-
W.S. CENTRAL	1,810	2,304	1	527	621	6	5	5	247
Ark.	68	60	-	50	50	4	-	2	31
La.	344	426	-	64	116	1	1	1	7
Okla.	56	64	1	61	71	1	1	-	28
Tex.	1,342	1,754	-	352	384	-	3	2	181
MOUNTAIN	180	203	-	119	165	4	2	-	28
Mont.	-	4	-	8	14	-	1	-	16
Idaho	9	3	-	6	11	-	-	-	-
Wyo.	1	3	-	-	2	-	-	-	-
Colo.	43	51	-	7	14	1	-	-	-
N. Mex.	26	66	-	29	31	-	1	-	5
Ariz.	66	40	-	51	65	1	-	-	7
Utah	6	8	-	9	17	2	-	-	-
Nev.	29	28	-	9	11	-	-	-	-
PACIFIC	1,156	1,628	7	1,014	1,087	2	29	1	145
Wash.	41	54	-	37	58	-	1	-	1
Oreg.	33	29	2	41	49	1	-	1	-
Calif.	1,057	1,512	5	859	898	1	25	-	139
Alaska	1	7	-	20	13	-	1	-	5
Hawaii	24	26	-	57	69	-	2	-	-
Guam	-	-	U	3	2	-	-	-	-
P.R.	238	212	-	93	127	-	2	-	10
V.I.	6	8	-	2	1	-	-	-	-
Pac. Trust Terr.	-	-	U	-	-	-	-	-	-

U: Unavailable

TABLE IV. Deaths in 121 U.S. cities,* week ending April 7, 1984 (14th Week Ending)

Reporting Area	All Causes, By Age (Years)						P&I** Total
	All Ages	≥65	45-64	25-44	1-24	<1	
NEW ENGLAND	756	532	154	24	23	21	59
Boston, Mass.	178	119	37	5	10	5	24
Bridgeport, Conn.	53	37	11	2	2	1	3
Cambridge, Mass.	33	25	7	-	1	-	3
Fall River, Mass.	35	26	8	1	-	-	-
Hartford, Conn.	67	44	13	5	1	4	1
Lowell, Mass.	29	21	6	1	1	-	3
Lynn, Mass.	28	23	5	-	-	-	-
New Bedford, Mass.	25	21	4	-	-	-	1
New Haven, Conn.	67	43	14	2	4	4	1
Providence, R.I.	77	46	23	1	3	4	4
Somerville, Mass.	7	6	1	-	-	-	-
Springfield, Mass.	46	34	7	3	-	2	7
Waterbury, Conn.	33	26	5	2	-	-	3
Worcester, Mass.	78	61	13	2	1	1	9
MID. ATLANTIC	2,651	1,777	583	166	76	49	126
Albany, N.Y.	51	34	10	-	3	4	1
Allentown, Pa.	17	13	4	-	-	-	-
Buffalo, N.Y.	139	83	38	9	4	5	8
Camden, N.J.	53	38	10	1	2	2	1
Elizabeth, N.J.	33	24	8	1	-	-	5
Erie, Pa.†	36	26	10	-	-	-	4
Jersey City, N.J.	45	35	7	1	1	1	1
N.Y. City, N.Y.	1,398	940	287	114	33	24	60
Newark, N.J.	55	23	23	2	5	2	6
Paterson, N.J.	29	16	9	2	-	2	2
Philadelphia, Pa.†	358	226	88	19	18	7	15
Pittsburgh, Pa.†	69	46	16	3	2	2	2
Reading, Pa.	27	19	7	-	1	-	-
Rochester, N.Y.	119	91	19	5	4	-	8
Schenectady, N.Y.	30	23	4	3	-	-	-
Scranton, Pa.†	38	28	7	1	2	-	5
Syracuse, N.Y.	54	37	15	2	-	-	1
Trenton, N.J.	40	30	7	2	1	-	2
Utica, N.Y.	27	19	8	-	-	-	1
Yonkers, N.Y.	33	26	6	1	-	-	4
E.N. CENTRAL	2,224	1,431	538	116	58	81	96
Akron, Ohio	82	52	22	3	2	3	-
Canton, Ohio	41	30	9	-	1	1	2
Chicago, Ill	450	280	119	26	11	14	15
Cincinnati, Ohio	158	101	40	10	3	4	21
Cleveland, Ohio	149	88	40	9	6	6	2
Columbus, Ohio	126	76	34	7	3	6	6
Dayton, Ohio	121	78	30	4	3	6	2
Detroit, Mich.	262	163	68	15	7	9	12
Evansville, Ind.	48	35	8	1	1	3	-
Fort Wayne, Ind.	58	46	9	1	2	-	4
Gary, Ind.	14	8	4	2	-	-	-
Grand Rapids, Mich.	45	36	4	4	-	1	3
Indianapolis, Ind.	186	104	53	11	9	9	12
Madison, Wis.	30	19	5	5	-	1	-
Milwaukee, Wis.	147	103	27	4	4	9	5
Peoria, Ill.	59	40	9	2	2	6	3
Rockford, Ill.	47	33	10	4	-	-	5
South Bend, Ind.	38	28	7	2	1	-	2
Toledo, Ohio	100	68	24	4	1	3	2
Youngstown, Ohio	63	43	16	2	2	-	-
W.N. CENTRAL	690	497	122	33	19	19	38
Des Moines, Iowa	66	43	21	2	-	-	5
Duluth, Minn.	34	25	7	-	2	-	1
Kansas City, Kans.	31	23	3	4	1	-	3
Kansas City, Mo.	104	75	17	6	4	2	8
Lincoln, Nebr.	26	19	6	-	1	-	1
Minneapolis, Minn.	85	56	15	3	3	8	2
Omaha, Nebr.	73	55	12	3	3	-	5
St. Louis, Mo.	155	109	25	12	3	6	5
St. Paul, Minn.	72	57	9	1	2	3	2
Wichita, Kans.	44	35	7	2	-	-	6
S. ATLANTIC	1,150	665	283	105	44	52	59
Atlanta, Ga.	148	81	29	21	5	12	6
Baltimore, Md.	194	117	45	17	8	7	3
Charlotte, N.C.	75	41	17	14	1	1	4
Jacksonville, Fla.	106	68	30	2	4	2	8
Miami, Fla.	96	54	22	11	7	2	-
Norfolk, Va.	65	33	17	7	4	4	7
Richmond, Va.	90	50	29	4	3	4	10
Savannah, Ga.	27	18	6	2	1	-	2
St. Petersburg, Fla.	103	83	12	3	1	4	6
Tampa, Fla.	86	45	28	6	3	4	5
Washington, D.C.	135	61	40	16	6	12	7
Wilmington, Del.	25	14	8	2	1	-	1
E.S. CENTRAL	750	449	206	46	27	22	49
Birmingham, Ala.	109	61	35	5	6	2	4
Chattanooga, Tenn.	65	39	20	1	1	4	7
Knoxville, Tenn.	92	54	24	7	2	5	4
Louisville, Ky.	125	73	35	7	5	5	7
Memphis, Tenn.	143	90	35	10	6	2	16
Mobile, Ala.	39	26	7	3	2	1	2
Montgomery, Ala.	51	39	9	-	2	1	2
Nashville, Tenn.	126	67	41	13	3	2	7
W.S. CENTRAL	1,463	870	361	124	64	44	67
Austin, Tex.	69	38	19	4	3	5	4
Baton Rouge, La.	44	25	12	6	1	-	3
Corpus Christi, Tex.	39	24	12	2	-	1	-
Dallas, Tex.	179	98	49	17	9	6	5
El Paso, Tex.	71	40	18	5	5	3	5
Fort Worth, Tex.	101	71	21	6	1	2	9
Houston, Tex.	393	199	113	43	26	12	8
Little Rock, Ark.	85	59	16	2	2	6	11
New Orleans, La.	130	82	34	11	2	1	-
San Antonio, Tex.	171	121	32	11	5	2	11
Shreveport, La.	77	41	19	8	6	3	3
Tulsa, Okla.	104	72	16	9	4	3	8
MOUNTAIN	721	479	153	42	24	22	51
Albuquerque, N.Mex.	80	48	15	10	3	3	2
Colo. Springs, Colo.	34	28	3	2	-	1	8
Denver, Colo.	133	92	23	8	6	4	10
Las Vegas, Nev.	93	60	25	5	-	3	8
Ogden, Utah	24	16	7	-	-	1	2
Phoenix, Ariz.	153	99	38	7	6	3	5
Pueblo, Colo.	25	18	3	1	1	2	3
Salt Lake City, Utah	61	39	12	3	4	3	-
Tucson, Ariz.	118	79	27	6	4	2	13
PACIFIC	1,757	1,166	348	142	52	49	87
Berkeley, Calif.	23	13	5	2	2	1	-
Fresno, Calif.	94	56	25	5	3	5	10
Glendale, Calif.	19	16	1	1	1	-	-
Honolulu, Hawaii	56	31	18	2	2	3	5
Long Beach, Calif.	90	60	22	3	1	4	4
Los Angeles, Calif.	473	296	87	55	20	15	-
Oakland, Calif.	71	48	15	7	1	-	3
Pasadena, Calif.	19	15	3	1	-	-	3
Portland, Oreg.	105	75	19	7	1	3	6
Sacramento, Calif.	74	53	15	2	2	2	4
San Diego, Calif.	150	103	30	6	4	7	21
San Francisco, Calif.	136	83	29	18	3	3	4
San Jose, Calif.	172	118	33	10	7	4	11
Seattle, Wash.	165	109	32	19	3	2	8
Spokane, Wash.	64	54	5	4	1	-	5
Tacoma, Wash.	46	36	9	-	1	-	3
TOTAL	12,162††	7,866	2,748	798	387	359	632

* 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.

Rocky Mountain Spotted Fever — Continued

Instead, when a tick bite occurs, the patient and the family should be educated about the incubation period of RMSF (3-12 days) and the most common symptoms, and should be instructed to seek medical attention promptly if RMSF symptoms occur. No vaccine against RMSF is currently available.

Reference

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Epidemiologic Notes and Reports

Sulfur Dioxide Exposure in Portland Cement Plants

Complaints of burning eyes, sore throat, and chest tightness by workers in two Portland cement plants led to requests for Health Hazard Evaluations (HHE) conducted by the National Institute for Occupational Safety and Health (NIOSH). The nature of the symptoms, the combustion processes involved, and measurable levels of sulfur dioxide (SO_2) suggested possible exposure to SO_2 as the cause of the problems at each plant.

The production of Portland cement begins by crushing and milling sources of calcium, aluminum, and silica, which are then fused in rotary kilns at 1,450 C (2,642 F) and ground into cement powder. The raw materials are fed into the upper end of long, slightly inclined, cylindrical kilns, and fuel is blown into the lower end. Exhaust gases and fugitive dust emissions leave the kilns at the upper end and pass through dust-collection mechanisms called baghouses. These consist of a series of filters in the form of long cloth tubes or bags that collect particulate matter before the air is discharged up exhaust stacks. SO_2 is produced when the fuel source (e.g., coal, which is the primary fuel in the United States [*1*]) contains sulfur. Plants producing Portland cement have unique processes and design characteristics, and the concentrations of environmental contaminants fluctuate, depending on weather conditions and the amount of production. Therefore, SO_2 levels may vary from plant to plant and from day to day. Results of the NIOSH investigations follow.

Iowa: On January 16, 1980, NIOSH received an HHE request from the labor union representing cement workers at a Portland cement plant in Mason City, Iowa. Some workers, especially among the labor and maintenance crews, had experienced burning eyes, sore throat, chest tightness, cough, headache, nausea, frequent colds, shortness of breath, and dizziness for 5-6 months. The NIOSH team took samples for possible exposures to SO_2 emanating from the kiln exhaust system; analysis showed SO_2 concentrations ranging up to 1.03 parts per million (ppm). The coal burned in this plant had a mean total sulfur content of 0.7%.

Oklahoma: On June 6, 1981, NIOSH received an HHE request from a labor union representing workers at a Portland cement plant in Tulsa, Oklahoma. Complaints among workers had included eye or nose irritation, sore throat, dizziness, headache, and chest pain or tightness for 6-8 months. Samples taken at various locations around the plant showed SO_2 concentrations from 0.2 ppm to 1.8 ppm. The coal burned in these kilns had a mean sulfur content of 1.6%.

Reported by Div of Respiratory Disease Studies, National Institute for Occupational Safety and Health, CDC.

Editorial Note: Workers engaged in occupations involving exposures to SO_2 greater than 10 ppm show evidence of mucous-membrane irritation and reflex bronchoconstriction with increased airway resistance (*2-5*). The current Occupational Safety and Health Administration standard for occupational exposure to SO_2 establishes a permissible exposure limit (PEL) of 5 ppm as an 8-hour time-weighted average. In 1980, the American Conference of Governmental Industrial Hygienists (ACGIH) recommended lowering the PEL to 2 ppm, because, although

Sulfur Dioxide Exposure — Continued

SO_2 may not produce subjective irritation in acclimatized workers, it can cause bronchoconstriction and a temporary decrease in pulmonary function (*6*). ACGIH also recommends a 15-minute, short-term exposure limit of 5 ppm. Based on studies indicating chronic respiratory disease among workers exposed to 1-4 ppm SO_2, NIOSH recommends a 10-hour time-weighted exposure limit of 0.5 ppm (*7*). No effects were noted among steel workers exposed to a mean SO_2 concentration of 0.35 ppm (*8*).

In both investigations reported here, area samples were collected only in locations suspected of having elevated SO_2 concentrations, thus representing the worst case conditions for the particular shift sampled. Highest SO_2 concentrations at both facilities were found around the baghouses. Because the HHEs were conducted over short periods (1-2 days), changes in concentration due to process variations, atmospheric conditions, or the sulfur content of the kiln fuel could not be detected. In addition, samples were collected over 5-6 hours and reflect the average concentration during this period (*9*).

In a stratified, randomized cross-sectional study of the Portland cement industry previously conducted by NIOSH, 92 samples for SO_2 were collected from 13 plants. Only one sample exceeded 0.5 ppm, the NIOSH-recommended exposure criterion. Thus, SO_2 concentrations in Portland cement plants appear to be generally below levels documented to cause acute mucous-membrane irritation or to exacerbate chronic respiratory disease. However, the results reported above demonstrate that these workers are potentially exposed to SO_2 from the exhaust gases of kilns, especially those fueled by coal containing sulfur.

Workers at Portland cement facilities, particularly those burning fuel containing sulfur, should be aware of the acute and chronic effects of exposure to SO_2, and peak and full-shift concentrations of SO_2 should be periodically measured.

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Salmonella dublin and Raw Milk Consumption — California

In 1981, 46 cases of human *Salmonella dublin* infection were reported in California, and in 1982, 70 cases were reported. In both years, 24% of patients reported using certified raw milk (CRM). In 1983, 123 *S. dublin* cases were identified—the most ever reported in a single year—and of the 99 persons providing information on raw milk use, 44% reported using CRM.

The demographic characteristics and risk factors for *S. dublin* patients have consistently differed from those infected with other *Salmonella* serotypes. *S. dublin* patients are much older, and many have underlying, debilitating disorders. In 1983, 61% of *S. dublin* patients

Salmonella dublin — *Continued*

were 40 years of age or over, and 17% were less than 20 years of age. By contrast, salmonellosis caused by other serotypes is generally a pediatric disease, with 60% of infections occurring among individuals under age 20. At least 24 of the 1983 *S. dublin* patients had cancer, particularly lymphoma and leukemia; five had acquired immunodeficiency syndrome (AIDS); and others had diabetes mellitus, were immunodeficient, or were taking systemic corticosteroids and/or other immunosuppressants for a variety of disorders. Nearly 80% were hospitalized, and 26% died.

S. dublin gave continued evidence of being a particularly invasive serotype, as 79% of the 1983 isolates were recovered from extra-intestinal (nonfecal) sites, principally from blood, but also from cerebrospinal fluid, peritoneal fluid, and lung. By contrast, only 10%-15% of *Salmonella* isolates from all other serotypes in any year are from extra-intestinal sites. The invasiveness of *S. dublin* does not simply reflect the older age of the infected host: when controls infected by other *Salmonella* serotypes were matched by age and sex to *S. dublin* patients, the percentage of controls with positive extra-intestinal cultures remained below 15%.

To evaluate the possibility that (1) raw-to-rare beef or liver or (2) raw milk may be sources of *S. dublin* infection, the 1983 patients were asked about these food exposures: 16% reported consuming raw-to-rare beef or liver, whereas 44% reported using CRM. Raw milk use among persons with infections due to other *Salmonella* serotypes was 8% in a previous study. Raw milk represents less than 1% of all market milk distributed in California.

Since 1977, nearly 200 *Salmonella* isolates have been made from CRM by 14 local, state, and federal laboratories. Antibiogram tests of human *S. dublin* isolates have shown a statistically significant association between the patterns of isolates recovered from CRM users and the antibiogram patterns of isolates recovered from CRM itself.

The risk of contracting *S. dublin* from CRM in California has been estimated: assuming that 12,000 gallons of CRM are produced per day and that each user drinks 1 pint daily, the rate of *S. dublin* disease for CRM users in 1983 was estimated at 458.3 per million population. This contrasts with a rate of 2.9 per million for *S. dublin* patients from the California population that did not report drinking raw milk. The relative risk of illness from *S. dublin* for CRM users was, therefore, 158.0 (458.3/2.9). The association between CRM ingestion and *S. dublin* disease in 1983 was about 15 times stronger than the well-accepted association between cigarette smoking and lung cancer. Just as the majority of smokers do not develop lung cancer, the majority of raw milk users apparently do not develop *S. dublin* disease. The number of *S. dublin* cases in California is not larger than it is because the population that drinks CRM is very small, and the contamination of CRM appears intermittent. Salmonellosis from raw milk is a potential hazard that merits greater appreciation by consumers, producers, and health-care providers.

Adapted from California Morbidity *(March 30, 1984) by SB Werner, MD, FR Morrison, DrPH, GL Humphrey, DVM, RA Murray, DrPH, J Chin, MD, State Epidemiologist, California Dept of Health Svcs; Div of Bacterial Diseases, Center for Infectious Diseases, CDC.*

Editorial Note: Raw milk/milk products have been repeatedly demonstrated as the vehicles for a variety of human pathogens, including *Campylobacter, Streptococcus zooepidemicus,* and *Salmonella* of many different serotypes. Although the California data relate to illnesses associated with infection with a single *Salmonella* serotype, data collected in other states document that raw milk continues to be responsible for a substantial percentage of sporadic enteric illnesses, as well as for occasional outbreaks (*1-3*).

Currently available *S. dublin* data are most useful in determining a relative risk of infection to raw milk drinkers, since *S. dublin* is a strongly host-adapted serotype to cattle, and since there is good information concerning the quantity of raw milk produced in California. This calculation of a relative risk in CRM users is one of the first attempted in an endemic situation. The magnitude of the estimated relative risk is high, perhaps because many of the raw milk

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users are already very ill and may be more susceptible to infection and subsequent serious disease, even from a small inoculum.

Certification of raw milk is a copyrighted designation that requires adherence to certain quality-control procedures, but it does not imply the milk is free of pathogens, such as *Salmonella*. The report from California and a previous report of campylobacteriosis (*1*) both dealt with disease associated with the consumption of CRM.

In 1979-1980, *Salmonella dublin* infections in the remainder of the United States were similar to those in California in 1983 in many respects, including the strong association with consumption of raw milk (*2*), indicating that this problem is not localized to California. In both studies, patients with *S. dublin* infections tended to be older and have underlying illnesses more often than patients with isolates of other *Salmonella* serotypes and, in addition, experienced higher rates of hospitalization and mortality. Previous outbreaks of *S. dublin* infections in Oregon and Washington State were also traced to consumption of raw milk (*2,4*).

Data concerning only *S. dublin* isolates underestimate the extent of disease associated with raw milk consumption. Not only are there likely to be *S. dublin* infections that are not confirmed microbiologically, serotypes of *Salmonella* other than *S. dublin* can also cause milkborne disease. Outbreaks of illness among consumers of raw milk due to *S. typhimurium* in Arizona (*5*), Oregon (*3*), and Quebec (*6*), indicate that varying but occasionally large proportions of infections caused by this very common *Salmonella* serotype may be associated with consumption of raw dairy products. In recognition of this and the economic burden of milkborne salmonellosis, Scotland banned the sale and distribution of raw milk in 1983 (*7,8*).

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Unusual Syndrome with Fatalities among Premature Infants: Association with a New Intravenous Vitamin E Product

Since March 9, 1984, CDC has received reports from two hospitals of clusters of an unusual illness occurring among low-birthweight (less than 1,500 grams), premature infants in neonatal intensive-care units. Thirteen affected infants in these two hospitals developed clinically significant ascites, in addition to some or all of the following abnormalities: hepatomegaly, splenomegaly, cholestatic jaundice, azotemia, and thrombocytopenia. Eight infants have died. All affected infants had received parenteral nutrition therapy, in addition to other supportive measures and therapeutic interventions common to the care of low-birthweight infants. An intravenous vitamin E preparation, containing 25 mg/ml vitamin E, 9% polysorbate 80 and 1% polysorbate 20 in 2-ml vials (E-Ferol Aqueous Solution®, distributed by O'Neal,

Unusual Syndrome with Fatalities – Continued

Jones & Feldman, St. Louis, Missouri), was introduced in each hospital for addition to parenteral nutrition solutions approximately 1 month before the onset of illness in the first infant in both clusters. All affected infants received E-Ferol; some affected infants received up to 1 ml or more daily. Both outbreaks ceased shortly after use of E-Ferol was discontinued.

In collaboration with the state health departments, CDC is conducting ongoing epidemiologic investigations at both institutions. Although the etiology and pathophysiology of this syndrome are presently unclear, the U.S. Food and Drug Administration (FDA) and CDC recommend that E-Ferol not be used. FDA and the distributor have initiated a voluntary recall of the product. The product, which has been marketed since December 1983, is not the subject of an Approved New Drug Application by FDA.

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Editorial Note: Premature neonates are reported to have a relative deficiency of vitamin E at birth, which has been associated with hemolytic anemia in premature infants (*1*). Although vitamin E is reported to have a therapeutic benefit in treating this form of hemolytic disease in premature infants and may have a role in preventing the development of retrolental fibroplasia and bronchopulmonary dysplasia in infants requiring oxygen therapy, the benefit, risk, and dosage relationships are, at present, uncertain (*1,2*).

Other vitamin E preparations are available for enteral, subcutaneous, and intramuscular administration. Vitamin E is a component, at lower concentrations, of multivitamin preparations for intravenous use. Use of these alternative vitamin E preparations has not been temporally associated with the severe clinical syndrome described above. However, other complications, such as cholestatic jaundice, have been associated with total parenteral nutrition therapy (*3*) and thrombocytopenia with lipid emulsion therapy (*4*).

Additional reports of similar severe illness should be reported through appropriate state health officials to the Epidemiology Development Branch, Division of Drug and Biologic Experience, FDA (301) 443-6410 or the Hospital Infections Program, Center for Infectious Diseases, CDC (404) 329-3406.

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The data in this report are provisional, based on weekly reports to CDC by state health departments. The reporting week concludes at close of business on Friday; compiled data on a national basis are officially released to the public on the succeeding Friday.

The editor welcomes accounts of interesting cases, outbreaks, environmental hazards, or other public health problems of current interest to health officials. Such reports and any other matters pertaining to editorial or other textual considerations should be addressed to: ATTN: Editor, *Morbidity and Mortality Weekly Report,* Centers for Disease Control, Atlanta, Georgia 30333.

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