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Current Trends

Rubella Vaccination during Pregnancy — United States, 1971-1982

From January 1971 to December 1982, 959 pregnant women who received rubella vaccine either within 3 months before or 3 months after their presumed dates of conception were reported to CDC. These women were followed prospectively to determine the risk of fetal abnormalities following exposure to the vaccine.

Cendehill and HPV-77 Vaccines: Before April 1979, data were collected on 538 women vaccinated during pregnancy with either Cendehill or HPV-77 rubella vaccines (*1*). The outcomes of conception (live birth, stillbirth, and spontaneous or induced abortion) were known for 143 (96%) of the 149 women known to be susceptible at the time of vaccination. Ninety-four (66%) of these 143 women carried their pregnancies to term. All gave birth to infants free of defects compatible with congenital rubella syndrome (CRS)* (*2*), although eight infants had serologic evidence of intrauterine infection (*1,3*). Follow-up from 2 to 7 years of these eight infants indicates no problems compatible with CRS. An additional 196 infants born to women who either were immune (22) or of unknown immune status (174) at the time of vaccination were also free of such defects. Three other women (one susceptible, one immune, and one of unknown immune status) received unknown strains of rubella vaccine. All three delivered normal-appearing, healthy infants.

RA 27/3 Vaccine: Since licensure of the RA 27/3 rubella vaccine in 1979, 418 women who received it during pregnancy have been reported to CDC (Table 1). Outcomes of pregnancy are known for 390 (93%) women. Of the 111 women known to be susceptible at

*Defined as any two complications listed in A or one from A and one from B:

A. Cataracts/congenital glaucoma (either or both count as one), congenital heart disease, loss of hearing, pigmentary retinopathy.

B. Purpura, splenomegaly, jaundice (with onset beginning 24 hours after birth), microcephaly, mental retardation, meningoencephalitis, radiolucent bone disease.

TABLE 1. Pregnancy outcomes for 418 recipients of RA 27/3 vaccine — United States, through December 31, 1982

Prevaccination immunity status	Total women	Live births	Spontaneous abortions and stillbirths	Induced abortions	Outcome unknown
Susceptible	111	83*	3	19	8
Immune	24	22	1	0	1
Unknown	283	241†	7	17	19
Total	418	346	11	36	28

*Includes two twin births.
†Includes one twin birth.

Rubella Vaccination — Continued

the time of vaccination, 81 (73%) carried their pregnancies to term. The dates of vaccination and estimated dates of confinement were known for all of the 81 susceptible women who had full-term pregnancies (Figure 1). Twenty-eight women (35%) were vaccinated within 1 week before to 4 weeks after conception and 57 (70%) within 6 weeks before or 6 weeks after conception. Two hundred sixty-two other women elected to carry their pregnancies to term. Three had twin births (two to susceptible women and one to a woman of unknown immune status). While none of the 346 newborns whose mothers had been vaccinated had defects compatible with CRS, 11 were born with one or more congenital defects. The mothers of two of these infants were known to be susceptible at the time of vaccination; two were known to be immune; and seven were of unknown immune status.

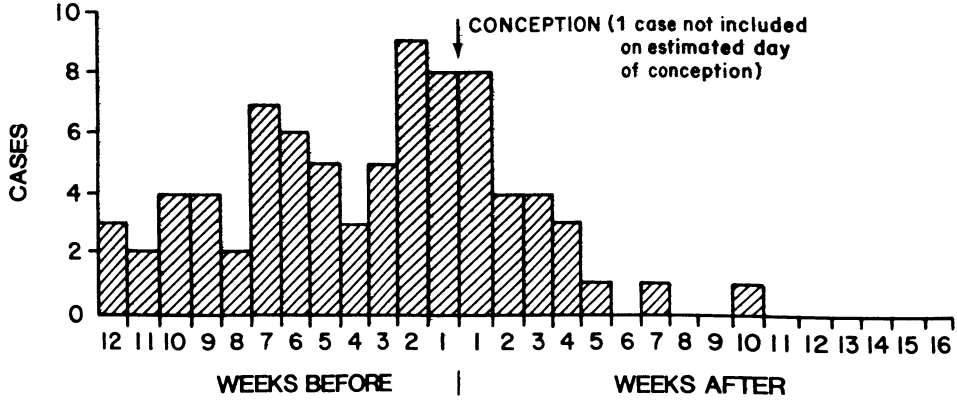
The two infants born to susceptible women had asymptomatic glandular hypospadias. Both had negative rubella-specific immunoglobulin (IgM) titers (less than 1:4) in cord blood at birth. A 6-month follow-up serum was available for one of the infants who had a rubella hemagglutination inhibition (HI) antibody titer of less than 1:8.

One of the two infants born to the immune women had multiple congenital anomalies; the other had a hydrocele that resolved spontaneously. Both had no detectable rubella-specific IgM antibodies at birth. Efforts to obtain follow-up sera have been unsuccessful.

Two of the seven infants born to the women whose immune status was unknown at the time of vaccination had heart murmurs that resolved spontaneously. A third infant had a spontaneously resolving hydrocele and hemangioma. Of the four remaining infants, one had asymptomatic glandular hypospadias; one had an omphalocele; one had hydrocephalus secondary to aqueductal stenosis and is being worked up for trisomy 21 mosaicism; and one had a small ventricular septal defect and an ectopic anus. Serologic data are currently available on four of these seven infants; none have any evidence of rubella infection.

Serologic evaluation (rubella HI titers and specific IgM on cord or neonatal blood specimens) was performed on 69 (83%) of the 83 infants whose mothers were susceptible. One normal-appearing infant had a rubella-specific IgM antibody titer of 1:8 in cord blood and a corresponding HI titer of 1:128. At 2 months of age, the HI titer had decreased to 1:16. The infant had no evidence of defects compatible with CRS at birth or at the 18-month follow-up examination. Blood studies were also obtained on 150 of the 241 infants born to mothers whose immune status was unknown at the time of vaccination. One such infant had a rubella-specific IgM antibody titer of 1:16 in cord blood. Both mother and infant had HI titers of 1:32

FIGURE 1. Rubella vaccination among susceptible recipients of RA 27/3 vaccine, by estimated date of conception (DOC)* — United States, through December 31, 1982



*DOC estimated to be 14 days after first day of last menstrual period.

Rubella Vaccination — Continued

at the time of birth; the infant's HI titer was 1:32 at 4 months of age. This infant had no evidence of defects compatible with CRS at birth or at the 10-month follow-up examination. A serum specimen was not obtained at the 10-month visit.

To date, 11 women have had spontaneous abortions or stillbirths. Thirty-six others elected to have induced abortions (Table 1). Rubella virus has now been isolated from the products of conception in one (4%) of 28 cases involving susceptible women (15 cases reported to CDC and 13 from the literature) (*4-6*).

Reported by Birth Defects Br, Chronic Diseases Div, Center for Environmental Health; Surveillance and Investigations Section, Surveillance, Investigations, and Research Br, Div of Immunization, Center for Prevention Svcs, CDC.

Editorial Note: Since 1971, CDC has maintained a register to monitor and quantitate the risks to the fetus following exposure to attenuated rubella vaccine virus. Data are obtained through reports from physicians and from state and local health departments, as well as directly from women vaccinated either within 3 months before or 3 months after conception. The patients are followed prospectively to determine the outcome of pregnancy. In 1979, when RA 27/3 rubella vaccine replaced the other rubella vaccines, concern was raised that it might have greater potential for teratogenicity than earlier vaccines. As with the other vaccines, data collected so far show no evidence that the RA 27/3 rubella vaccine can cause defects compatible with CRS. While hypospadias has been noted in CRS cases (*7,8*), there are no data to suggest that glandular hypospadias should be considered a CRS-associated defect.

Twenty-eight (35%) of the 81 susceptible mothers were vaccinated with the RA 27/3 vaccine during the highest risk period for viremia and fetal defects (1 week before to 4 weeks after conception) (*9,10*). Neither those infants nor any others were born with CRS; therefore, the observed risk of CRS following rubella vaccination continues to be zero. The theoretical maximum risk for the occurrence of CRS in this group of 83 children, however, based on the 95% confidence limits of the binomial distribution, may be as high as 5%. (If the 95 infants exposed to the other rubella vaccines are included, the maximum theoretical risk is 2%.) This overall maximum risk remains far less than the 20% or greater risk of CRS associated with maternal infection with wild rubella virus during the first trimester of pregnancy (*3*).

The occurrence of any congenital defect following maternal vaccination deserves careful analysis and follow-up. If only susceptibles are considered, the overall birth-defect rate is approximately 2% (2/83), which is less than the reported 4%-5% rate of birth defects in the absence of exposure to rubella vaccine recently noted by CDC (*11,12*). Neither of the two infants with congenital deformities born to women known to be susceptible at the time of vaccination had any evidence of rubella infection. The absence of rubella-specific IgM antibodies at birth was confirmed by the absence of HI antibodies after 6 months of age in the one infant tested.

While no CRS-like defects have been noted, it is clear that rubella vaccine viruses, including the RA 27/3 strain, can cross the placenta and infect the fetus. Approximately 2% of infants born to susceptible vaccinees had serologic evidence of subclinical infection, regardless of vaccine strain (*3*). On the other hand, while the rubella virus isolation rate from the products of conception for the RA 27/3 vaccine is only 4% (1/28), the rate for Cendehill and HPV-77 vaccines is 20% (17/85) (*3*). These data indicate that the risk of placental or fetal infection from RA 27/3 vaccine is minimal.

Following an earlier review of these data, the Immunization Practices Advisory Committee (ACIP) stated in 1981 that (*13*): (1) pregnancy remains a contraindication to rubella vaccination because of the theoretical, albeit small, risks of CRS; (2) reasonable precautions be taken to preclude vaccination of pregnant women, including asking women if they are pregnant, excluding those who say they are, and explaining the theoretical risks to the others; and (3) if

Rubella Vaccination — Continued

vaccination does occur within 3 months of conception, the risk of CRS is so small as to be negligible; thus, rubella vaccination of a pregnant woman should not in itself indicate interruption of pregnancy. The patient and her physician, however, should make the final decision. Data collected through 1982 continue to support these recommendations.

Since the inception of its vaccine-in-pregnancy register, CDC has encouraged reporting of all such cases. Because of the increasing number of cases reported to CDC, the experience with known susceptibles is becoming well defined. Therefore, CDC now encourages reporting only cases involving women known to have been susceptible at the time of vaccination. Laboratory services for serologic determination and culture of placental and fetal tissue will continue to be available at CDC for susceptible cases that are reported.

References

1. CDC. Rubella vaccination during pregnancy—United States, 1971-1981. MMWR 1982;31: 477-81.
2. Bureau of State Services. Rubella surveillance, January 1976-December 1978. HHS Publication No. (CDC) 80-8023. Atlanta, Georgia: Center for Disease Control, 1980:27.
3. Preblud SR, Stetler HC, Frank JA Jr, Greaves WL, Hinman AR, Herrmann KL. Fetal risk associated with rubella vaccine. JAMA 1981;246:1413-7.
4. Banatvala JE, O'Shea S, Best JM, Nicholls MV, Cooper K. Transmission of RA27/3 rubella vaccine strain to products of conception (letter). Lancet 1981;1:392.

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

Disease	33rd Week Ending			Cumulative, 33rd Week Ending		
	August 20, 1983	August 21, 1982	Median 1978-1982	August 20, 1983	August 21, 1982	Median 1978-1982
Aseptic meningitis	557	362	362	4,833	4,235	3,215
Encephalitis: Primary (arthropod-borne & unspec.)	80	47	50	776	724	570
Post-infectious	1	1	2	58	58	142
Gonorrhea: Civilian	17,840	18,903	21,139	558,408	599,217	616,951
Military	469	437	446	15,303	17,246	17,246
Hepatitis: Type A	340	459	569	13,437	14,026	17,441
Type B	433	446	381	14,220	13,439	10,890
Non A, Non B	60	49	N	2,135	1,453	N
Unspecified	168	203	203	4,909	5,437	6,366
Legionellosis	9	23	N	456	336	N
Leprosy	6	8	4	161	134	120
Malaria	17	21	21	482	658	658
Measles: Total	12	14	54	1,175	1,167	11,788
Indigenous	12	N	N	979	N	N
Imported*	-	N	N	196	N	N
Meningococcal infections: Total	48	36	33	1,954	2,093	1,870
Civilian	48	36	33	1,939	2,081	1,855
Military	-	-	-	15	12	14
Mumps	69	28	66	2,379	4,136	6,925
Pertussis	80	54	46	1,351	867	874
Rubella (German measles)	6	69	65	747	1,942	3,151
Syphilis (Primary & Secondary): Civilian	666	678	640	20,360	20,837	16,481
Military	5	9	6	260	267	202
Toxic-shock syndrome	5	N	N	269	N	N
Tuberculosis	480	476	543	14,665	15,928	17,079
Tularemia	12	8	7	199	146	129
Typhoid fever	10	14	14	239	243	297
Typhus fever, tick-borne (RMSF)	58	33	49	854	716	730
Rabies, animal	119	140	133	3,869	4,038	4,038

TABLE II. Notifiable diseases of low frequency, United States

	Cum. 1983		Cum. 1983
Anthrax	-	Plague	27
Botulism: Foodborne (Alaska 1)	13	Poliomyelitis: Total	4
Infant	38	Paralytic (Ind. 1)	4
Other	-	Psittacosis (Calif. 1)	76
Brucellosis (Pa. 1, Va. 2, Ala. 1, Okla. 1, Tex. 4)	126	Rabies, human	2
Cholera	1	Tetanus (Upstate N.Y. 1, Fla. 1)	47
Congenital rubella syndrome	16	Trichinosis	24
Diphtheria	-	Typhus fever, flea-borne (endemic, murine) (Tex. 2)	32
Leptospirosis (Mich. 1, Okla. 1)	31		

*None of the 12 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 August 20, 1983 and August 21, 1982 (33rd week)

Reporting Area	Aseptic Meningitis	Encephalitis		Gonorrhea (Civilian)		Hepatitis (Viral), by type				Legionellosis	Leprosy	Malaria
		Primary	Post-infectious			A	B	NA,NB	Unspecified			
	1983	Cum. 1983	Cum. 1983	Cum. 1983	Cum. 1982	1983	1983	1983	1983	1983	Cum. 1983	Cum. 1983
UNITED STATES	557	776	58	558,408	599,217	340	433	60	168	9	161	482
NEW ENGLAND	20	30	-	14,273	14,321	3	12	1	10	-	3	24
Maine	2	-	-	714	672	-	2	1	-	-	-	1
N.H.	-	4	-	449	500	2	1	-	-	-	2	-
Vt.	1	1	-	262	268	-	-	-	-	-	-	1
Mass.	7	13	-	6,127	6,585	1	7	-	10	-	-	11
R.I.	2	-	-	763	971	-	2	-	-	-	-	3
Conn.	8	12	-	5,958	5,325	-	-	-	-	-	1	8
MID ATLANTIC	52	73	5	71,390	74,013	27	66	6	12	-	20	68
Upstate N.Y.	16	19	-	11,018	11,777	5	25	3	4	-	-	20
N.Y. City	1	9	-	28,957	31,152	9	8	-	-	-	19	19
N.J.	23	15	-	13,342	13,341	9	26	3	8	-	-	22
Pa.	12	30	5	18,073	17,743	4	7	-	-	-	1	7
E.N. CENTRAL	172	233	18	77,736	86,005	52	46	3	13	2	5	35
Ohio	32	72	7	21,422	23,808	41	11	2	2	1	1	5
Ind.	65	69	1	7,805	9,687	2	9	1	5	-	-	-
Ill.	2	15	7	19,745	24,492	7	5	-	1	-	2	13
Mich.	73	59	-	21,689	20,321	2	20	-	5	1	2	14
Wis.	-	18	3	7,075	7,697	-	1	-	-	-	-	3
W.N. CENTRAL	17	61	7	25,483	28,106	17	11	2	5	2	5	20
Minn.	-	19	1	3,683	4,161	5	1	-	1	-	4	6
Iowa	10	31	-	2,920	2,968	-	2	2	-	-	-	3
Mo.	2	7	-	12,063	13,196	4	2	-	3	2	-	2
N. Dak.	-	-	-	275	380	-	-	-	-	-	-	2
S. Dak.	1	-	2	712	767	8	-	-	-	-	-	1
Nebr.	2	3	-	1,627	1,707	-	4	-	1	-	-	1
Kans.	2	1	4	4,203	4,927	-	2	-	-	-	1	5
S. ATLANTIC	76	119	15	144,991	156,294	28	76	11	13	1	8	69
Del.	-	-	-	2,593	2,499	-	-	-	-	-	-	-
Md.	13	16	-	18,329	19,303	-	12	3	3	-	1	13
D.C.	1	-	-	9,992	8,858	-	1	-	-	-	-	9
Va.	11	25	2	12,833	12,713	6	12	-	1	-	1	13
W. Va.	2	12	-	1,515	1,753	2	-	-	-	-	-	1
N.C.	21	30	-	21,966	24,737	5	7	-	2	-	-	3
S.C.	-	2	-	13,853	15,189	3	5	-	2	1	-	5
Ga.	5	6	1	29,256	29,982	2	14	1	-	-	1	5
Fla.	23	28	12	34,654	41,260	10	25	7	5	-	5	20
E.S. CENTRAL	47	28	1	46,762	51,326	21	19	4	3	-	-	7
Ky.	7	-	-	5,498	6,938	9	2	-	2	-	-	-
Tenn.	7	6	-	19,197	20,206	3	4	-	1	-	-	-
Ala.	28	19	-	14,484	15,104	6	11	4	-	-	-	5
Miss.	5	3	1	7,583	9,078	3	2	-	-	-	-	2
W.S. CENTRAL	86	96	2	80,416	82,366	64	52	1	80	-	19	46
Ark.	-	6	-	6,042	6,784	4	1	1	9	-	-	1
La.	-	8	-	15,558	14,964	6	4	-	1	-	1	4
Okla.	19	24	1	9,288	9,086	11	17	-	2	-	-	9
Tex.	67	58	1	49,528	51,532	43	30	-	68	-	18	32
MOUNTAIN	24	37	4	17,672	20,390	29	23	3	7	-	12	23
Mont.	-	-	-	749	846	-	2	-	-	-	-	-
Idaho	-	-	-	759	935	1	1	-	-	-	-	2
Wyo.	3	2	-	464	585	-	-	-	-	-	-	1
Colo.	16	19	-	5,035	5,493	5	3	1	-	-	2	8
N. Mex.	-	1	-	2,145	2,651	1	-	-	-	-	-	5
Ariz.	3	7	4	4,967	5,450	13	7	1	4	-	9	4
Utah	2	8	-	841	972	4	3	-	-	-	1	3
Nev.	-	-	-	2,712	3,458	5	7	1	3	-	-	-
PACIFIC	63	99	6	79,685	86,396	99	128	29	25	4	89	190
Wash.	6	7	1	6,011	7,142	6	10	2	-	-	12	5
Oreg.	-	-	2	4,318	4,957	15	2	3	-	-	1	6
Calif.	55	85	3	65,671	70,593	76	116	24	25	4	52	179
Alaska	1	-	-	2,072	2,131	2	-	-	-	-	-	-
Hawaii	1	7	-	1,613	1,573	-	-	-	-	-	24	-
Guam	U	-	-	74	97	U	U	U	U	U	-	2
P.R.	4	-	1	1,663	1,856	-	3	-	4	-	-	2
V.I.	U	-	-	160	174	U	U	U	U	U	-	-
Pac. Trust Terr.	U	-	-	-	294	U	U	U	U	U	-	-

N: Not notifiable U: Unavailable

TABLE III. (Cont.'d). Cases of specified notifiable diseases, United States, weeks ending August 20, 1983 and August 21, 1982 (33rd week)

Reporting Area	Measles (Rubeola)					Menin-gococcal Infections	Mumps			Pertussis			Rubella		
	Indigenous		Imported*		Total										
	1983	Cum. 1983	1983	Cum. 1983	Cum. 1982	Cum. 1983	1983	Cum. 1983	Cum. 1982	1983	Cum. 1983	Cum. 1982	1983	Cum. 1983	Cum. 1982
UNITED STATES	12	979	-	196	1,167	1,954	69	2,379	4,136	80	1,351	867	6	747	1,942
NEW ENGLAND	-	2	-	13	13	98	3	95	156	1	43	36	-	10	14
Maine	-	-	-	-	-	8	-	15	36	-	4	3	-	-	-
N.H.	-	-	-	3	2	3	1	18	13	-	6	4	-	2	8
Vt.	-	-	-	-	2	7	-	14	7	-	7	2	-	3	-
Mass.	-	2	-	2	3	32	1	23	70	-	21	15	-	5	2
R.I.	-	-	-	-	-	8	-	12	14	1	5	10	-	-	1
Conn.	-	-	-	8	6	40	1	13	16	-	-	2	-	-	3
MID ATLANTIC	3	67	-	24	154	324	6	188	257	6	273	147	1	134	91
Upstate N.Y.	1	1	-	8	109	102	3	71	58	3	89	71	1	25	44
N.Y. City	2	40	-	12	37	56	3	32	44	-	41	21	-	86	31
N.J.	-	26	-	1	4	55	-	33	36	-	16	16	-	3	16
Pa.	-	-	-	3	4	111	-	52	119	3	127	39	-	20	-
E.N. CENTRAL	-	556	-	56	72	369	3	1,172	2,233	6	277	203	-	107	174
Ohio	-	72	-	13	1	115	-	536	1,556	-	86	53	-	2	-
Ind.	-	384	-	4	2	44	1	32	37	1	33	15	-	23	27
Ill.	-	98	-	33	24	105	-	120	248	1	99	88	-	45	65
Mich.	-	2	-	5	45	66	2	419	294	4	21	15	-	15	48
Wis.	-	-	-	1	-	39	-	65	98	-	38	32	-	22	34
W.N. CENTRAL	-	-	-	-	49	109	2	136	537	5	86	43	-	30	55
Minn.	-	-	-	-	-	16	2	27	416	1	33	16	-	6	5
Iowa	-	-	-	-	-	12	-	35	30	-	5	5	-	-	-
Mo.	-	-	-	-	2	54	-	21	9	-	12	10	-	-	38
N. Dak.	-	-	-	-	-	3	-	-	-	-	1	-	-	-	-
S. Dak.	-	-	-	-	-	4	-	-	1	1	5	4	-	-	1
Nebr.	-	-	-	-	3	1	-	2	-	-	-	1	-	-	-
Kans.	-	-	-	-	44	19	-	51	81	3	30	7	-	24	11
S. ATLANTIC	7	163	-	26	37	405	3	154	235	10	179	159	2	91	69
Del.	-	-	-	-	-	-	-	8	10	-	3	5	-	-	1
Md.	4	6	-	4	2	42	1	24	24	-	14	36	-	1	33
D.C.	-	-	-	-	1	4	-	-	-	-	-	1	-	-	-
Va.	-	10	-	13	14	59	-	29	32	-	45	18	1	2	12
W. Va.	-	-	-	-	3	2	1	35	88	-	5	5	-	-	1
N.C.	-	-	-	1	-	82	1	8	11	3	21	19	-	10	1
S.C.	-	-	-	4	-	42	-	8	13	-	13	16	-	1	1
Ga.	-	8	-	-	-	67	-	42	12	5	54	29	-	11	6
Fla.	3	139	-	4	17	107	-	-	45	2	24	30	1	66	14
E.S. CENTRAL	-	1	-	5	7	122	-	46	39	1	18	33	-	11	44
Ky.	-	-	-	1	1	26	-	21	12	1	6	5	-	10	26
Tenn.	-	-	-	-	6	42	-	20	15	-	5	16	-	-	2
Ala.	-	1	-	4	-	37	-	2	6	-	3	3	-	1	-
Miss.	-	-	-	-	-	17	-	3	6	-	4	9	-	-	16
W.S. CENTRAL	-	39	-	34	36	212	48	198	162	34	268	59	1	102	89
Ark.	-	5	-	7	-	17	-	2	6	-	15	3	-	-	1
La.	-	-	-	25	2	43	45	45	5	1	6	9	-	9	1
Okla.	-	1	-	-	20	25	-	-	-	29	192	3	-	-	3
Tex.	-	33	-	2	14	127	3	151	151	4	55	44	1	93	84
MOUNTAIN	-	1	-	3	11	70	-	96	78	7	136	53	-	29	75
Mont.	-	-	-	-	-	8	-	2	3	-	1	1	-	5	5
Idaho	-	-	-	-	-	6	-	6	3	-	5	10	-	8	6
Wyo.	-	-	-	-	1	2	-	-	2	1	6	2	-	2	7
Colo.	-	-	-	2	8	25	-	10	15	4	88	14	-	-	6
N. Mex.	-	-	-	-	-	6	-	-	-	-	10	5	-	-	6
Ariz.	-	-	-	1	2	14	-	68	33	-	14	20	-	6	14
Utah	-	-	-	-	-	8	-	6	16	2	12	1	-	7	20
Nev.	-	1	-	-	-	1	-	4	6	-	-	-	-	1	11
PACIFIC	2	150	-	35	788	245	4	294	439	10	71	134	2	233	1,331
Wash.	-	1	-	4	39	33	-	38	61	3	13	20	-	9	37
Oreg.	-	7	-	2	6	37	-	-	-	-	6	23	-	13	6
Calif.	2	141	-	27	738	166	4	229	364	7	51	77	2	210	1,276
Alaska	-	-	-	2	1	2	-	12	6	-	-	-	-	1	5
Hawaii	-	1	-	-	4	7	-	15	8	-	1	14	-	-	7
Guam	U	1	U	1	6	1	U	-	3	U	-	-	U	-	2
P.R.	-	81	-	-	90	11	6	109	50	-	9	17	-	3	8
V.I.	U	-	U	5	-	-	U	-	1	U	-	-	U	2	-
Pac. Trust Terr.	U	-	U	-	-	-	U	-	5	U	-	-	U	-	-

*For measles only, imported cases includes both out-of-state and international importations. U: Unavailable †International §Out-of-state

TABLE III. (Cont.'d). Cases of specified notifiable diseases, United States, weeks ending August 20, 1983 and August 21, 1982 (33rd week)

Reporting Area	Syphilis (Civilian) (Primary & Secondary)		Toxic-shock Syndrome	Tuberculosis		Tula-remia	Typhoid Fever	Typhus Fever (Tick-borne) (RMSF)	Rabies, Animal
	Cum. 1983	Cum. 1982	1983	1983	Cum. 1983	Cum. 1983	Cum. 1983	Cum. 1983	Cum. 1983
UNITED STATES	20,360	20,837	5	480	14,665	199	239	854	3,869
NEW ENGLAND	433	354	-	12	420	4	10	6	20
Maine	13	1	-	-	27	-	-	-	5
N.H.	16	3	-	1	29	-	-	1	2
Vt.	2	1	-	-	9	-	-	-	1
Mass.	270	242	-	10	218	3	8	2	7
R.I.	14	19	-	-	28	1	-	-	-
Conn.	118	88	-	1	109	-	2	3	5
MID ATLANTIC	2,537	2,893	2	84	2,639	-	40	22	156
Upstate N.Y.	146	308	-	24	439	-	6	5	51
N.Y. City	1,540	1,734	-	33	1,064	-	16	1	-
N.J.	502	394	-	16	554	-	13	8	14
Pa.	349	457	2	11	582	-	5	8	91
E.N. CENTRAL	1,031	1,262	2	77	1,975	2	39	61	336
Ohio	300	196	1	6	303	-	11	39	40
Ind.	80	125	1	19	201	-	2	4	26
Ill.	461	696	-	46	881	1	17	12	178
Mich.	140	182	-	-	490	1	9	6	8
Wis.	50	63	-	6	100	-	-	-	84
W.N. CENTRAL	238	358	1	13	468	62	13	42	589
Minn.	96	71	-	-	92	-	2	-	106
Iowa	12	18	-	-	39	-	-	-	151
Mo.	89	213	-	6	235	50	6	20	82
N. Dak.	2	7	-	-	5	-	-	1	56
S. Dak.	9	1	-	-	31	3	-	4	82
Nebr.	11	11	1	2	19	5	-	2	52
Kans.	19	37	-	5	47	4	5	15	60
S. ATLANTIC	5,394	5,607	-	119	2,980	13	33	354	1,324
Del.	22	9	-	-	27	-	-	3	2
Md.	349	306	-	9	245	5	5	34	555
D.C.	241	315	-	3	118	-	1	-	1
Va.	376	390	-	27	312	1	6	45	480
W. Va.	17	20	-	3	90	-	2	11	94
N.C.	506	418	-	28	428	6	2	145	16
S.C.	330	331	-	9	266	-	1	61	18
Ga.	999	1,151	-	13	555	1	2	52	139
Fla.	2,554	2,667	-	27	939	-	14	3	19
E.S. CENTRAL	1,398	1,439	-	34	1,312	14	4	59	267
Ky.	93	76	-	2	319	-	1	8	62
Tenn.	393	392	-	10	393	9	1	32	159
Ala.	558	528	-	14	346	-	1	16	46
Miss.	354	443	-	8	254	5	1	3	-
W.S. CENTRAL	5,451	5,372	-	56	1,710	87	31	304	768
Ark.	133	134	-	1	196	56	2	25	128
La.	1,190	1,218	-	-	242	2	3	-	20
Okla.	141	115	-	25	151	23	2	197	82
Tex.	3,987	3,905	-	30	1,121	6	24	82	538
MOUNTAIN	429	522	-	5	387	13	7	4	151
Mont.	5	3	-	-	34	3	1	1	66
Idaho	6	23	-	2	22	2	-	1	6
Wyo.	10	14	-	-	10	3	-	2	6
Colo.	100	145	-	-	49	1	1	-	15
N. Mex.	125	119	-	-	82	1	-	-	7
Ariz.	105	115	-	2	153	1	3	-	31
Utah	14	15	-	-	24	1	1	-	4
Nev.	64	88	-	1	13	1	1	-	16
PACIFIC	3,449	3,030	-	80	2,774	4	62	2	258
Wash.	113	102	-	8	148	2	3	-	2
Oreg.	86	71	-	5	119	1	3	-	1
Calif.	3,198	2,772	-	65	2,319	1	54	2	240
Alaska	7	8	-	-	36	-	-	-	15
Hawaii	45	77	-	2	152	-	2	-	-
Guam	-	1	U	U	3	-	-	-	-
P.R.	499	415	-	13	313	-	-	-	32
V.I.	12	21	U	U	1	-	-	-	-
Pac. Trust Terr.	-	-	U	U	-	-	-	-	-

U: Unavailable

TABLE IV. Deaths in 121 U.S. cities,* week ending August 20, 1983 (33rd week)

Reporting Area	All Causes, By Age (Years)						P&I** Total
	All Ages	≥65	45-64	25-44	1-24	<1	
NEW ENGLAND	606	395	139	37	17	18	37
Boston, Mass.	180	101	45	19	7	8	14
Bridgeport, Conn.	41	26	12	2	1	-	-
Cambridge, Mass.	22	18	2	-	1	1	-
Fall River, Mass.	28	21	5	1	1	-	-
Hartford, Conn.	42	25	14	2	1	-	2
Lowell, Mass.	25	18	5	1	1	-	1
Lynn, Mass.	15	12	3	-	-	-	-
New Bedford, Mass.	26	15	6	4	-	1	-
New Haven, Conn.	53	37	12	-	1	3	3
Providence, R.I.	47	33	8	3	1	2	5
Somerville, Mass.	9	7	2	-	-	-	-
Springfield, Mass.	40	24	14	1	-	1	9
Waterbury, Conn.	26	20	1	2	1	2	1
Worcester, Mass.	52	38	10	2	2	-	2
MID. ATLANTIC	2,373	1,503	543	194	67	66	93
Albany, N.Y.	59	40	12	2	2	3	1
Allentown, Pa.	22	16	6	-	-	-	-
Buffalo, N.Y.	114	75	24	9	4	2	7
Camden, N.J.	35	22	9	3	1	-	3
Elizabeth, N.J.	19	12	6	1	-	-	-
Erie, Pa.†	36	23	9	-	2	2	2
Jersey City, N.J.	40	29	5	4	1	1	-
N.Y. City, N.Y.	1,326	826	302	127	36	35	51
Newark, N.J.	55	25	18	9	1	2	2
Paterson, N.J.	35	18	12	4	-	1	2
Philadelphia, Pa.†	205	128	38	19	14	6	7
Pittsburgh, Pa.†	49	32	15	2	-	-	-
Reading, Pa.	32	27	5	-	-	-	1
Rochester, N.Y.	127	81	32	5	3	6	6
Schenectady, N.Y.	23	15	6	2	-	-	-
Scranton, Pa.†	22	16	5	-	-	1	1
Syracuse, N.Y.	103	65	25	4	3	6	2
Trenton, N.J.	29	22	7	-	-	-	3
Utica, N.Y.	21	17	2	2	-	-	2
Yonkers, N.Y.	21	14	5	1	-	1	3
E.N. CENTRAL	2,118	1,294	544	142	57	79	64
Akron, Ohio	59	36	13	4	3	3	-
Canton, Ohio	35	24	7	2	1	1	1
Chicago, Ill	520	293	146	54	7	20	9
Cincinnati, Ohio	115	72	29	6	1	7	13
Cleveland, Ohio	175	91	63	11	5	5	5
Columbus, Ohio	137	77	41	8	4	7	1
Dayton, Ohio	97	54	32	6	2	3	3
Detroit, Mich.	255	159	61	19	7	9	6
Evansville, Ind.	30	21	6	1	1	1	1
Fort Wayne, Ind.	44	27	13	-	1	3	1
Gary, Ind.	21	5	8	5	1	2	1
Grand Rapids, Mich.	43	25	8	7	1	2	1
Indianapolis, Ind.	151	94	35	6	11	5	1
Madison, Wis.	28	18	7	1	1	1	2
Milwaukee, Wis.	126	96	22	-	2	6	5
Peoria, Ill. §	43	37	-	1	2	1	3
Rockford, Ill.	32	22	8	1	1	-	2
South Bend, Ind.	49	32	12	1	3	1	2
Toledo, Ohio	90	63	17	5	3	2	7
Youngstown, Ohio	68	48	16	4	-	-	-
W.N. CENTRAL	660	426	140	36	28	29	19
Des Moines, Iowa	54	38	9	4	3	-	2
Duluth, Minn.	22	13	5	1	2	1	1
Kansas City, Kans.	31	22	5	1	2	1	1
Kansas City, Mo.	108	65	24	10	3	5	3
Lincoln, Nebr.	21	17	3	1	-	-	-
Minneapolis, Minn.	105	63	28	2	6	6	2
Omaha, Nebr.	65	41	16	5	2	1	3
St. Louis, Mo.	130	92	21	7	2	8	4
St. Paul, Minn.	71	46	16	1	4	4	-
Wichita, Kans.	53	29	13	4	4	3	3
S. ATLANTIC	1,218	741	313	83	37	44	38
Atlanta, Ga.	120	62	33	14	5	6	3
Baltimore, Md.	299	185	76	22	8	8	7
Charlotte, N.C.	78	49	20	5	1	3	3
Jacksonville, Fla.	79	48	20	3	4	4	6
Miami, Fla.	96	46	35	7	2	6	1
Norfolk, Va.	45	33	6	-	2	4	4
Richmond, Va.	71	44	20	4	2	1	2
Savannah, Ga.	52	32	14	3	1	2	5
St. Petersburg, Fla.	76	61	13	1	-	1	4
Tampa, Fla.	76	40	23	5	3	5	-
Washington, D.C.	182	112	44	16	6	4	3
Wilmington, Del.	44	29	9	3	3	-	-
E.S. CENTRAL	635	394	157	41	17	25	16
Birmingham, Ala.	93	55	24	7	4	3	2
Chattanooga, Tenn.	57	42	12	2	-	1	2
Knoxville, Tenn.	50	34	8	2	2	4	-
Louisville, Ky.	121	81	28	8	1	3	3
Memphis, Tenn.	133	73	40	9	6	4	3
Mobile, Ala.	48	32	11	1	2	2	4
Montgomery, Ala.	37	19	8	6	1	3	-
Nashville, Tenn.	96	58	26	6	1	5	2
W.S. CENTRAL	1,324	770	323	121	66	44	35
Austin, Tex.	36	22	11	2	1	-	-
Baton Rouge, La.	53	33	13	6	1	-	4
Corpus Christi, Tex.	30	15	8	4	2	1	-
Dallas, Tex.	210	117	46	26	11	10	1
El Paso, Tex.	50	29	12	1	7	1	2
Fort Worth, Tex.	73	46	19	3	3	2	2
Houston, Tex.	348	184	86	43	25	10	8
Little Rock, Ark.	82	46	24	6	4	2	4
New Orleans, La.	118	65	30	15	4	4	-
San Antonio, Tex.	182	108	52	8	6	8	10
Shreveport, La.	42	29	9	1	-	3	1
Tulsa, Okla.	100	76	13	6	2	3	3
MOUNTAIN	586	352	149	46	16	23	26
Albuquerque, N.Mex.	75	42	20	9	3	1	3
Colo. Springs, Colo.	35	22	10	2	1	-	4
Denver, Colo.	116	67	33	8	5	3	4
Las Vegas, Nev.	68	35	25	5	1	2	2
Ogden, Utah	15	7	4	1	2	1	1
Phoenix, Ariz.	132	81	34	6	4	7	2
Pueblo, Colo.	21	17	3	1	-	-	3
Salt Lake City, Utah	52	34	5	6	-	7	2
Tucson, Ariz.	72	47	15	8	-	2	5
PACIFIC	1,601	1,048	331	112	61	45	85
Berkeley, Calif.	18	15	2	1	-	-	-
Fresno, Calif.	86	52	18	5	6	4	7
Glendale, Calif.	18	14	3	1	-	-	1
Honolulu, Hawaii	52	32	12	5	2	1	2
Long Beach, Calif.	80	52	16	3	3	6	2
Los Angeles, Calif.	372	252	72	31	10	7	13
Oakland, Calif.	67	39	16	6	4	2	1
Pasadena, Calif.	36	26	7	-	1	2	2
Portland, Oreg.	125	84	22	8	5	4	5
Sacramento, Calif.	75	45	17	6	4	3	12
San Diego, Calif.	132	80	35	9	5	3	14
San Francisco, Calif.	134	83	31	13	2	5	1
San Jose, Calif.	166	107	32	14	10	3	11
Seattle, Wash.	142	101	30	6	4	1	7
Spokane, Wash.	57	39	11	-	4	2	6
Tacoma, Wash.	41	27	7	4	1	2	1
TOTAL	11,121††	6,923	2,639	812	366	373	413

* 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.

§ Data not available. Figures are estimates based on average of past 4 weeks.

Rubella Vaccination — Continued

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Update: Chloroquine-Resistant *Plasmodium falciparum* — Africa

The first confirmed cases of chloroquine-resistant *Plasmodium falciparum* acquired in Africa were reported in 1978 (*1*) and occurred in non-immune travelers who had been in East Africa for relatively short periods of time. These reports of chloroquine-prophylaxis or treatment failures were substantiated by serial parasitologic and clinical observations of each infection and, when available, in-vitro confirmation of drug resistance. CDC continues to monitor the status of chloroquine-resistant *P. falciparum* malaria in East Africa (*2*). Recent reports document that the transmission of resistant parasites is now occurring more widely in Africa than was previously described (*2*).

During the past year, confirmed chloroquine-resistant infections have been described from specific areas in Zambia (*3*) and Sudan (*4*); previously, Kenya, Tanzania, Uganda, Madagascar, and the Comoros Islands were acknowledged to have transmission of chloroquine-resistant *P. falciparum*. It remains unclear whether these countries have nationwide transmission of disease and whether contiguous countries are similarly affected. In addition, a few apparent chloroquine-resistant infections have been reported in Malawi and northeastern Zaire. It may now be prudent to advise travelers to these specific suspect areas that they may be at risk of acquiring chloroquine-resistant malaria. While such anecdotal reports may reflect the spread of chloroquine-resistant *P. falciparum* in Africa, they require further confirmation; great caution should be exercised in interpreting case reports of drug-resistant malaria.

Studies in several West African countries, as well as a recent assessment of drug susceptibility of *P. falciparum* infections in western and central Zaire, have failed to demonstrate chloroquine resistance (*5*). These experiences emphasize the importance of rigorously applying accurate drug-susceptibility testing procedures and adhering to the accepted World Health Organization definitions of drug resistance (*6*).

Since health professionals frequently advise travelers of health risks that may be incurred during travel, they should be aware of the changing distribution of chloroquine-resistant malaria in Africa. CDC has published recommendations for malaria chemoprophylaxis for travelers to affected areas of East Africa (*2*); *Fansidar* (sulfadoxine 500 mg plus pyrimethamine 25 mg) one tablet weekly PLUS chloroquine 300 mg (base) once weekly* is currently

*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.

Plasmodium falciparum – Continued

recommended. Weekly doses of Fansidar and chloroquine may be taken together on the same day. It should be noted, however, that this combination may not be completely effective in preventing episodes of symptomatic malaria, as prophylaxis failures with sulfonamide-antifolate combination drugs have occurred (*7,8*). Travelers should be advised that any acute febrile illness may be malaria and that medical attention should be sought, regardless of whether chemoprophylaxis is being taken.

Further updates of this rapidly evolving situation will be published as accurate information becomes available. An expanded discussion of the recommendations for the prophylaxis of malaria is available in *Prevention of Malaria in Travelers, 1982* (*9*).

Reported by Malaria Br, Div of Parasitic Diseases, Center for Infectious Diseases, CDC.

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Epidemiologic Notes and Reports

Valproate: A New Cause of Birth Defects — Report from Italy and Follow-Up from France

Studies by the Indagine Policentrica Italiana sulle Malformazioni Congenite (IPIMC) in 1980-1982 found a significant association between valproic-acid exposure during the first trimester of pregnancy and spina bifida (Table 2). Among 118 infants with spina bifida, two (1.7%) were exposed to valproic acid; in the group with other malformations, three (0.1%) of 4,489 were exposed.

Further data from France on the association between spina bifida aperta among infants with birth defects and valproic-acid use during the first trimester update the preliminary report from Lyon (Tables 3 and 4) (*1*). An infant with spina bifida, who had intrauterine exposure to valproic acid, has been added, and an infant with spina bifida, whose mother had not

TABLE 2. Association between spina bifida (SB) and maternal treatment with valproic acid (VA) among malformed neonates registered with the Indagine Policentrica Italiana sulle Malformazioni Congenite – Italy

	SB	Other malformations	Total
VA treatment	2	3	5
No VA treatment	116	4,486	4,602
Total	118	4,489	4,607

Odds ratio = 25.8; 95% confidence limits, 3.0-191.0; $p < 0.001$

Valproate – Continued

been recognized as having epilepsy, has been properly classified. These data represent the cumulative experience during 1976 and from 1978 to December 1982.

Reported by Bolletino Epidemiologica Nazionale (November 25, 1982); E Robert, MD, Institut Europeen des Genomutations, Lyon, France; Birth Defects Br, Chronic Diseases Div, Center for Environmental Health, CDC.

Editorial Note: In addition to these new data from Italy and France, a United Kingdom researcher has reported that, of infants born to 196 pregnant women treated with valproic acid, 157 (80%) were normal and nine (5%) had spina bifida (2). The remaining 30 infants had other structural defects, including cardiovascular defects, orofacial clefts, and digital abnormalities. Since most of the pregnancies were reported either to the U.K. researcher or to a drug company and since normal pregnancies would tend not to be reported, there is probably some bias in the direction of reporting abnormal pregnancies. Given that these data were collected before the report from France and that spina bifida accounted for 23% (9/39) of the reported abnormalities, the 10-fold excess reported from the United Kingdom is probably not due entirely to reporting bias.

With these new data, valproic acid and sodium valproate should be considered human teratogens. CDC has estimated that a pregnant woman in the United States treated with these drugs would have a 1%-2% risk of having a child with spina bifida.* Since this risk is similar to the risk of spina bifida recurrence in subsequent pregnancies, women exposed in the first trimester should consult their physicians about further prenatal counseling. A pregnant woman undergoing treatment for epilepsy should not change her drug therapy without first consulting her physician.

Little is known about the relationship between valproic acid and other birth defects. To better define the risk of such therapy, CDC is assembling a registry of women taking valproic acid during pregnancy. Physicians caring for such women are urged to report these pregnancies to the CDC registry as soon as possible by calling (404) 452-4035 on weekdays between 8 a.m. and 4:30 p.m., Eastern time, or by writing the Birth Defects Branch, Chronic Diseases Division, Center for Environmental Health, Centers for Disease Control, Atlanta, Georgia 30333.

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*Estimate based on the Bayse theorem.

TABLE 3. Association between spina bifida aperta (SBA) and treatment with valproic acid (VA) of mothers who delivered infants with birth defects – Lyon, France

	SBA	Other birth defects	Total
VA treatment	10	21	31
No VA treatment	140	7,566	7,706
Total	150	7,587	7,737

Odds ratio = 25.7; 95% confidence limits, 10.9-58.6; $p < 0.001$

TABLE 4. Association between spina bifida aperta (SBA) and treatment with valproic acid (VA) of mothers who have seizure disorders and who delivered infants with birth defects – Lyon, France

	SBA	Other birth defects	Total
VA treatment	10	21	31
No VA treatment	2	41*	43
Total	12	62	74

Odds ratio = 9.8; 95% confidence limits, 1.7-70.0; $p = < 0.002$

*Five with unknown treatment; three with no treatment.

Erratum: Vol. 32, No. 28

p. 370. In the article, "Behavioral Risk Factor Prevalence Surveys—United States, Second Quarter 1982," the data reported in Table 2, Item 7, "Drinking and Driving, Montana," on p. 371 should read:

Risk factor, by state	Age group (years) by sex 18-34 M	18-34 F	35-54 M	35-54 F	≥55 M	≥55 F	All ages M	All ages F	Total respondents Number	Total respondents Rate
7. Drinking & driving¶¶										
Montana***	41.7	18.8	22.3	5.6	7.4	1.7	28.4	9.1	500	18.5

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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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