SUMMARY
January 1976 – December 1978 (Issued May 1980)

CENTER FOR DISEASE CONTROL

RUBELLA

SURVEILLANCE

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES • Public Health Service

PREFACE

This report summarizes information received from state and local health departments and other pertinent sources. Much of the information is preliminary. It is intended primarily for the use of those with responsibility for disease control activities.

Contributions to the Surveillance Report are welcome. Please address to:

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SUGGESTED CITATION
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**Also Chief, Perinatal Virology Branch, Virology Division, Bureau of Laboratories

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I. INTRODUCTION

The objective of the rubella immunization program is to prevent fetal infection. This objective can be achieved by vaccination of 2 target groups: 1) preschool and elementary school children of both sexes and 2) adolescent and adult females. In 1969 when the rubella vaccine was first licensed, it was decided that the major emphasis of the U.S. rubella immunization program would be vaccination of the former group. Because age-specific rubella rates were highest in the younger age groups, it was reasoned that pregnant women could be protected from exposure to disease by eliminating disease in children, who were the principal reservoir and transmitters of infection. Secondary emphasis was placed on selective vaccination of women of childbearing age. Ten years later, it appears that this vaccine strategy has successfully prevented rubella epidemics that probably would have occurred in the early 1970s. Unfortunately, the reported decrease in rubella rates has occurred largely for children and not for the older age groups.

The problem has not been with the strategy itself, but rather with its implementation. Increased emphasis needs to be placed on vaccinating unimmunized prepubertal, adolescent, and adult females. Only through this combined approach of vaccination of adults, particularly women of childbearing age, and the continued vaccination of all children will there be a decrease both in the number of susceptible pregnant women and in their risk of exposure to or contact with active cases of rubella (1). This combined approach is necessary since data from the United Kingdom indicate that selective vaccination of 11- to 14-year-old girls and postpubertal women at high risk of exposure to rubella has not resulted in a rapid reduction in reported cases of either rubella in women of childbearing age or congenital rubella (1,2).

This report summarizes selected U.S. epidemiologic data on rubella and congenital rubella.

II. RECENT TRENDS

A. Source of Data

Rubella and congenital rubella syndrome (CRS) did not become nationally reportable conditions until 1966; however, some states have maintained surveillance of these diseases for many years and have reported cases voluntarily to the Center for Disease Control (CDC). Therefore, in this surveillance report, data for years before 1966 were transmitted voluntarily by selected states; beginning in 1966, data were submitted as part of each state's Weekly Telegraphic Report of Notifiable Diseases. Although data received have varied considerably in completeness of reporting and diagnostic accuracy, they are adequate to show disease patterns and trends.

B. Reported Rubella

Rubella cases reported by each state for the years 1969-1978 are presented in Table 1. While the incidence of reported rubella has been fluctuating in recent years, the characteristic 6- to 9-year cycle of epidemic rubella activity has been interrupted; no peak has been seen in the United States since the 1964 epidemic (Figure 1, Figure 2). The 1978 total of 18,269 cases of rubella represents a 10.4% decrease in reported cases compared with the final number in 1977 (20,395), which, in contrast, was 63.3% higher than the number reported in 1976 (12,491 cases).

The seasonal pattern of rubella remains unchanged from year to year; disease incidence increases in January, peaks by April or May, and drops to a low level by August (Figure 3). Reported rubella incidence per 100,000 population varies in different regions, although part of this variation is due to differences in reporting (Figure 4).

TABLE 1
REPORTED CASES OF RUBELLA, BY STATE, 1969–1978

AREA	1969	1970	1971	1972	1973	1974	1975	1976	1977	1978
UNITED STATES*	**57,686**	**56,552**	**45,086**	**25,507**	**27,804**	**11,917**	**16,343**	**12,491**	**20,395**	**18,269**
NEW ENGLAND	**4,149**	**2,816**	**1,908**	**1,132**	**3,676**	**1,195**	**2,103**	**370**	**1,238**	**826**
Maine	426	551	302	87	79	302	43	16	70	158
New Hampshire	116	157	54	41	387	23	307	13	257	108
Vermont	122	69	102	77	49	43	72	6	65	51
Massachusetts	1,461	1,289	862	526	2,046	385	1,227	196	392	261
Rhode Island	329	130	111	97	200	20	28	7	136	42
Connecticut	1,695	620	477	304	915	422	428	132	318	206
MIDDLE ATLANTIC	**3,564**	**4,268**	**2,748**	**1,980**	**4,305**	**1,107**	**1,895**	**2,500**	**6,167**	**3,108**
Upstate New York								642	3,400	580
New York City	1,985	1,166	1,072	464	980	440	553	163	336	152
New Jersey	625	903	634	1,227	3,029	465	1,057	1,483	1,775	1,625
Pennsylvania	954	2,199	1,042	289	296	262	285	212	656	751
EAST NORTH CENTRAL	**13,275**	**11,447**	**9,512**	**6,297**	**6,659**	**3,845**	**4,827**	**4,891**	**4,619**	**8,995**
Ohio	1,407	2,187	1,064	452	711	529	649	435	1,096	1,390
Indiana	2,404	2,075	2,305	805	1,081	645	1,045	1,063	1,005	649
Illinois	1,825	1,871	1,396	1,163	1,264	635	414	1,376	754	1,972
Michigan	4,307	3,012	2,955	1,460	2,001	1,388	1,714	1,513	1,160	3,373
Wisconsin	3,332	2,302	1,792	2,417	1,665	648	1,005	504	604	1,611
WEST NORTH CENTRAL	**4,066**	**3,546**	**3,529**	**1,799**	**1,179**	**413**	**1,503**	**548**	**655**	**716**
Minnesota	245	107	291	502	224	18	37	36	27	128
Iowa	2,534	2,093	751	464	221	15	35	91	179	72
Missouri	569	571	1,546	500	264	183	753	139	93	118
North Dakota	237	138	102	59	233	19	71	3	25	83
South Dakota	...	4	98	13	24	26	18	21	89	112
Nebraska	366	574	100	58	141	6	21	3	3	34
Kansas	115	59	641	203	72	146	568	255	239	169
SOUTH ATLANTIC	**7,840**	**7,026**	**3,549**	**2,689**	**2,291**	**1,376**	**1,634**	**1,329**	**1,738**	**1,411**
Delaware	211	50	62	14	17	31	21	36	27	37
Maryland	789	339	166	66	10	5	38	5	4	305
District of Columbia	166	22	7	7	4	5	—	47	—	1
Virginia	1,744	782	229	67	547	67	326	247	585	247
West Virginia	2,428	1,425	725	450	347	317	240	328	174	342
North Carolina	19	49	53	34	204	57	45	18	454	204
South Carolina	300	685	461	51	80	685	780	593	239	32
Georgia	76	90	28	87	16	4	4	2	58	29
Florida	2,107	3,584	1,818	1,913	1,060	205	180	53	197	214
EAST SOUTH CENTRAL	**2,953**	**3,031**	**4,097**	**1,674**	**1,517**	**673**	**1,008**	**438**	**2,006**	**555**
Kentucky	1,193	984	1,756	915	428	223	245	193	95	155
Tennessee	1,624	1,549	2,025	578	645	359	730	229	1,790	215
Alabama	136	396	233	63	210	66	23	2	110	25
Mississippi	...	102	83	118	234	25	10	14	11	160
WEST SOUTH CENTRAL	**6,441**	**9,458**	**5,125**	**1,770**	**1,540**	**578**	**781**	**630**	**848**	**977**
Arkansas	200	46	337	37	119	25	20	190	4	58
Louisiana	39	160	298	96	100	178	285	92	30	494
Oklahoma	1,839	843	76	41	185	58	103	81	38	18
Texas	4,363	8,409	4,414	1,596	1,136	317	373	267	776	407
MOUNTAIN	**3,125**	**2,274**	**2,115**	**1,271**	**2,452**	**417**	**534**	**477**	**368**	**237**
Montana	107	344	126	36	529	27	253	236	15	22
Idaho	94	208	45	36	46	20	74	17	25	3
Wyoming	105	149	867	9	8	2	—	3	6	—
Colorado	1,423	469	311	539	1,589	177	139	31	194	53
New Mexico	321	237	251	128	174	130	20	4	11	4
Arizona	853	675	428	423	8	2	2	—	25	103
Utah	154	173	69	92	83	27	38	166	82	40
Nevada	68	19	18	8	15	32	8	20	10	12
PACIFIC	**12,273**	**12,686**	**12,503**	**6,895**	**4,185**	**2,253**	**2,058**	**1,308**	**2,756**	**1,444**
Washington	2,169	5,824	3,057	1,257	784	420	370	228	482	149
Oregon	734	1,017	810	465	811	242	221	143	141	174
California	7,682	5,498	8,381	5,084	2,541	1,572	1,446	913	1,694	1,100
Alaska	559	140	68	28	19	—	—	2	1	8
Hawaii	1,129	207	187	61	30	19	21	22	438	13
Guam	---	---	---	---	---	---	---	8	8	5
Puerto Rico	401	28	69	93	42	35	30	26	39	17
Virgin Islands	---	---	---	---	---	---	---	15	2	1
Pacific Tr. Terr.	---	---	---	---	---	---	---	---	---	3

*Excludes U.S. Territories
—No Cases Reported
---Data Not Available
Source: Reported Cases of Notifiable Diseases in the United States, Morbidity & Mortality Annual Supplements for Respective Years

Fig.1 RUBELLA INCIDENCE IN 10 SELECTED AREAS* UNITED STATES, 1928–1978

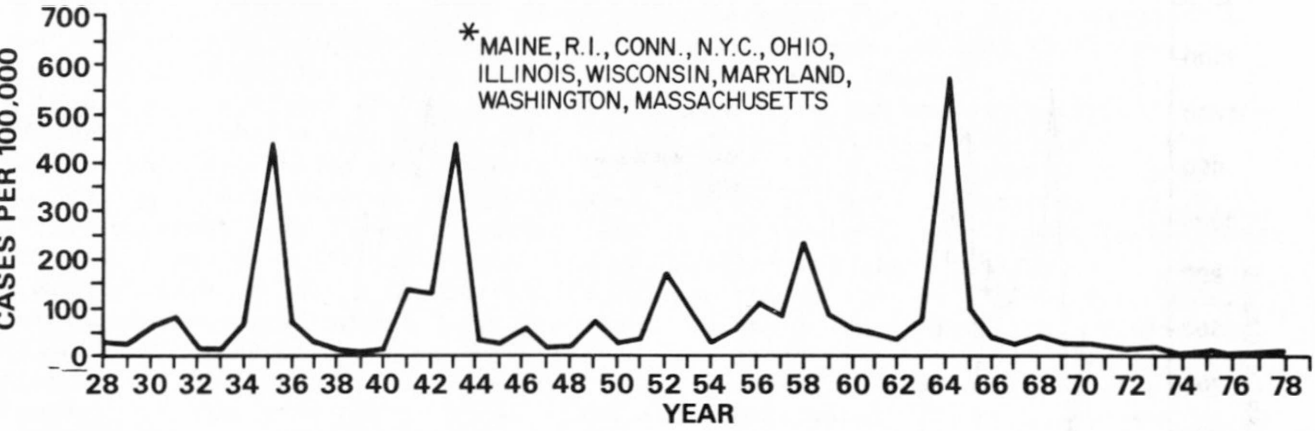
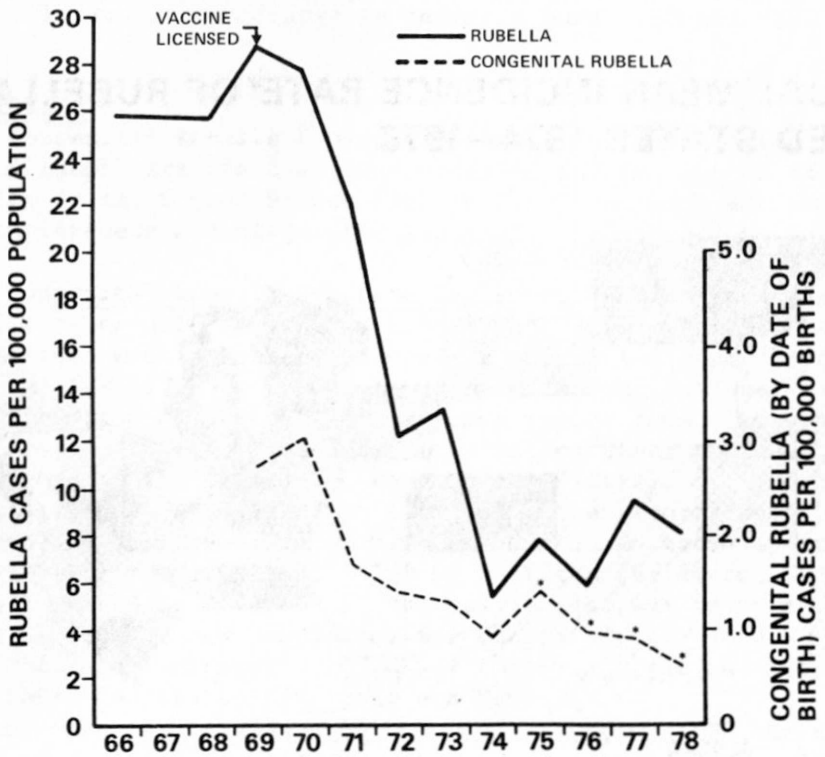


Fig.2 REPORTED RUBELLA (BY YEAR OF REPORT) AND CONGENITAL RUBELLA (BY YEAR OF BIRTH) CASES, BY YEAR, UNITED STATES, 1966–1978



*REPORTING FOR RECENT YEARS IS INCOMPLETE, AS SOME CASES ARE NOT DIAGNOSED UNTIL LATER IN CHILDHOOD

Fig. 3 RUBELLA CASES, BY WEEK OF REPORT, UNITED STATES

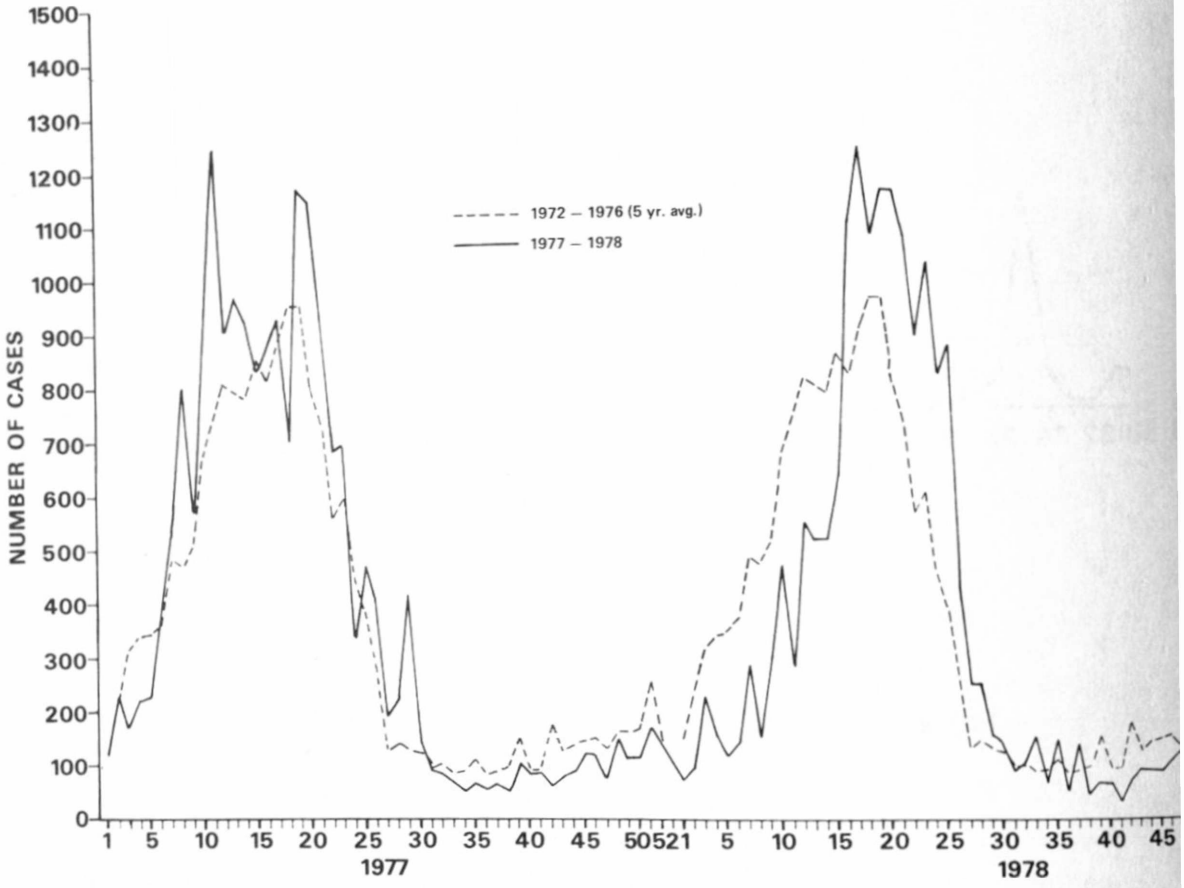
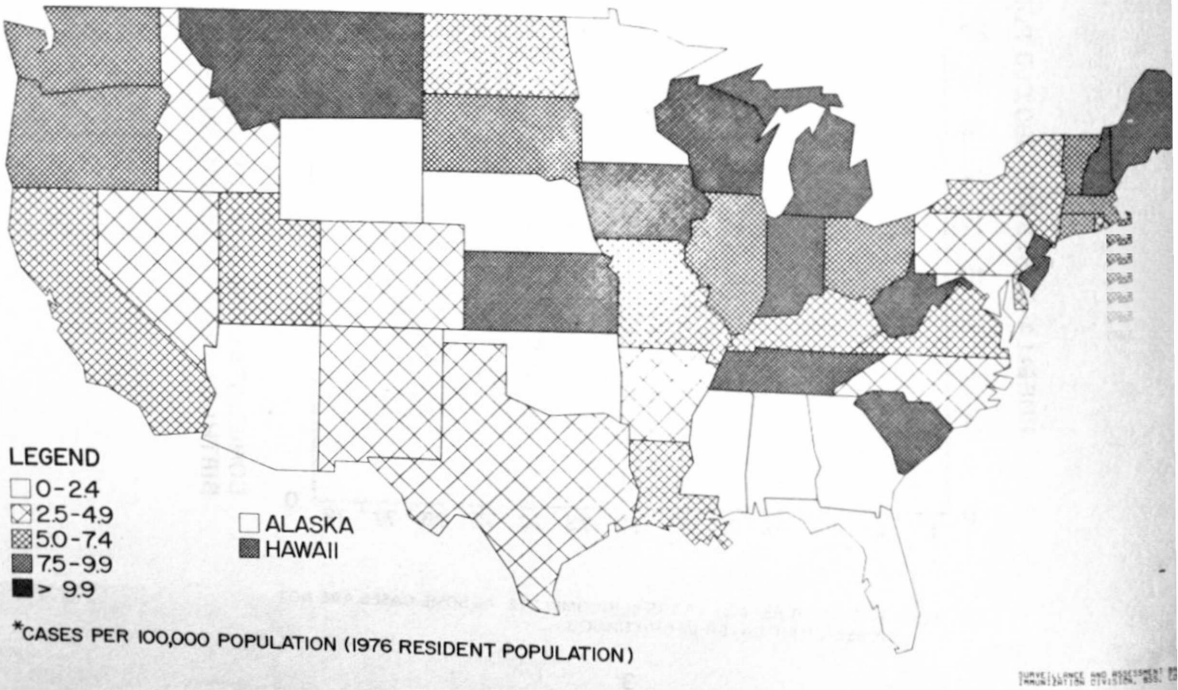


Fig. 4 ANNUAL MEAN INCIDENCE RATE* OF RUBELLA, BY S
UNITED STATES, 1974–1978



*CASES PER 100,000 POPULATION (1976 RESIDENT POPULATION)

C. Age-Specific Incidence of Rubella

Since the primary emphasis of the U.S. rubella immunization program has been vaccination of children in the 1- to 12-year age group, the greatest decreases in reported rubella have been seen for persons under 15 years of age; little decline has been noted in the 15-year-and-older group (Table 2, Figure 5, Figure 6). Although the incidence declined modestly for the older age groups shortly after the licensure of rubella vaccine in 1969, 15- to 19-year-olds have recently had the highest rate of rubella and, together with those over 19 years, have made up an increasingly large proportion of all cases (Figure 7, Table 2, Table 3). Between 1975 (the first year in which age-specific data became available from a large number of states) and 1977, the incidence rate of reported rubella increased, with the greatest increase in the 20- to 24- (74.7%) and the 25- to 29- (81.8%) year-olds. The highest reported attack rate, previously in the 5- to 9-year-olds, occurred in those 15-19 years of age (Figure 6, Figure 7). In 1977, as in 1976, slightly more than 70% of the rubella cases reported by age occurred in persons 15 years and older (Table 3). This same age group accounted for approximately 62% of such cases in 1975 but less than 25% of these cases in prevaccine years (3).

The age-specific data available for 1978 indicate that rubella continues to be a problem in older individuals, with those 15-19 years of age still having the greatest incidence rate (Table 3). Only the 20- to 24-year age group experienced an increased rate (34.3%) of rubella infection between 1977 and 1978. The risk of rubella for persons 20 years and older is substantially greater than it was in 1975: about 2.5 times as great for those 20-24 years old, and approximately 1.5 times as great for those 25 years of age and older. These general observations are also apparent when comparing the 1978 data with the yearly average for 1975-1977 (Figure 8).

These findings are consistent with the observation that outbreaks of rubella continue to occur in secondary schools, colleges, military installations, and places of employment, most notably hospitals (1,4). It is clear that women of childbearing age must be more effectively vaccinated to decrease further their risk of rubella infection.

D. Congenital Rubella

The National Congenital Rubella Syndrome Registry (NCRSR) and the Birth Defects Monitoring Program (BDMP) are the 2 major sources of information on the number of CRS cases occurring in the United States each year. Since both surveillance systems are limited by completeness and diagnostic accuracy, they should be interpreted with caution.

1. National Congenital Rubella Syndrome Registry. Along with rubella, CRS became a nationally reportable disease in 1966. Only the number of CRS cases is reported on the states' weekly telegraphic report. Detailed reports of CRS cases are submitted to the NCRSR. When a case is reported to the National Morbidity Reporting System without a completed registry case report form, the reporting source is contacted and encouraged to provide more information about the case. When appropriate, this case is then added to the registry listing.

Since the registry was established in 1969, 520 case reports have been submitted; 471 involved children born in 1969 or later. No case reports were submitted for children born in 1969 or later by 6 states (Delaware, Georgia, Nevada, Rhode Island, South Dakota, and Vermont), and only 1 case was reported by each of 6 other states (Alaska, Maine, New Hampshire, New Mexico, Oregon, and Wyoming). In contrast, a total of 245 case reports (52.0% of the total) was submitted by 5 states (California, Colorado, Louisiana, New York, and Texas).

To obtain a more accurate analysis of the registry cases, CDC has expanded and changed the criteria for classification of cases (Appendix 1). The classification of cases has been subdivided from 3 into 5 categories, and minor changes have been

Table 2

Percent Distribution of Reported Rubella Cases and Incidence Rate,* by Age Group, Illinois, Massachusetts, and New York City, 1966-1968,† 1969-1971,† and 1975-1977†

	1966-1968			1969-1971			1975-1977			Percent Change 1966-1968 to 1975-1977	
Age Group (Years)	No.	% of Total	Incidence Rate	No.	% of Total	Incidence Rate	No.	% of Total	Incidence Rate	% of Total	Incidence Rate
<5	1,294	21.6	63.3	768	21.5	37.6	160	9.8	9.8	-54.6	-84.5
5-9	2,304	38.5	101.3	1,253	35.1	55.3	223	14.2	11.6	-63.1	-88.5
10-14	1,020	17.0	44.0	572	16.0	24.6	229	13.9	11.2	-18.2	-74.5
15-19	759	12.7	35.7	610	17.1	28.7	634	38.7	27.4	+204.7	-23.2
20+	610	10.2	3.7	367	10.3	2.3	384	23.4	2.3	+129.4	-37.8
Total	5,987	100.0	24.3	3,570	100.0	14.4	1,640	100.0	6.7	-	-72.4

*Reported number of cases per 100,000 population

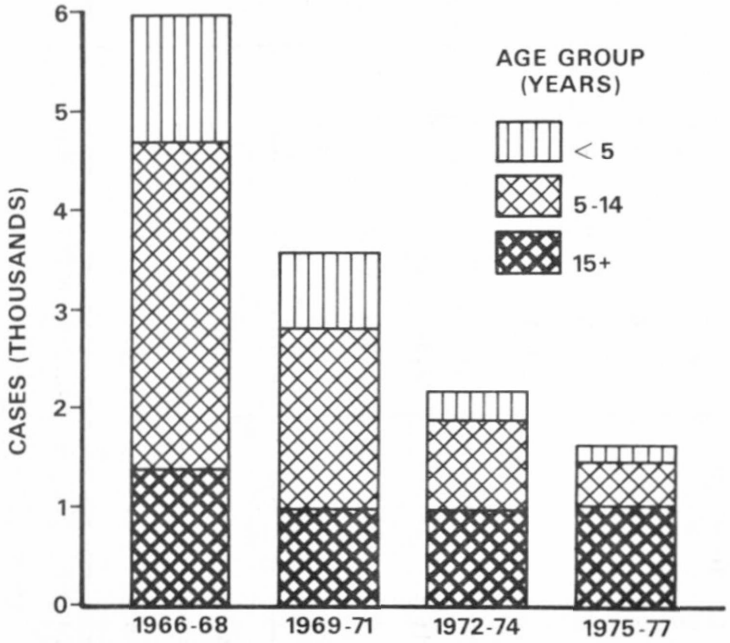
Table 5

Percent Distribution of Reported Rubella Cases and Incidence Rate*, by Age Group, United States, 1975-1978

Age (Years)	1975			1976			1977			1978			Percent Change 1977-1978	
	No.	%	Incidence Rate	No.	%	Incidence Rate	No.	%	Incidence Rate	No.	%	Incidence Rate	%	Rate
<5	1,016	12.2	12.8	684	10.2	8.3	941	7.8	10.4	786	7.6	9.0	-2.6	-13.5
5-9	938	11.3	10.9	629	9.4	6.8	1,012	8.4	10.0	619	6.0	6.5	-28.6	-35.0
10-14	1,209	14.6	11.9	651	9.8	6.2	1,610	13.3	14.2	1,051	10.2	10.0	-23.6	-29.6
15-19	3,836	46.2	36.8	2,927	43.8	25.9	5,867	48.6	47.0	4,543	44.1	38.3	-9.2	-18.5
20-24	900	10.8	9.5	1,128	16.9	10.9	1,950	16.1	16.6	2,540	24.7	22.3	+53.4	+34.3
25-29	182	2.2	2.2	344	5.2	3.6	346	2.9	4.0	363	3.5	3.6	+20.7	-10.0
30+	223	2.7	0.4	315	4.7	0.6	352	2.9	0.6	394	3.8	0.6	+31.0	0.0
Total with known age	8,304	49.9	-	6,678	53.4	-	12,078	59.2	-	10,296	56.4	-	-	-
Unknown age	8,348	50.1	-	5,813	46.6	-	8,317	40.8	-	7.973	43.6	-	-	-
TOTAL	16,652	100.0	7.8	12,491	5.8		20,395	100.0	9.4	18,269	100.0	8.4	-	-10.6

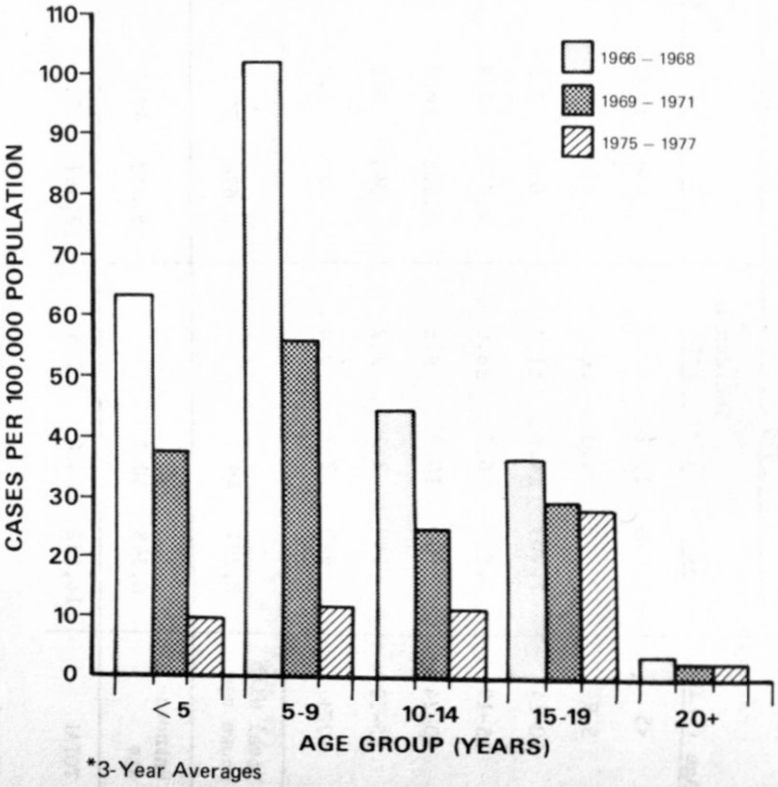
*Incidence rate = cases per 100,000 population extrapolated from the age distribution of cases reported by age from 40 (1975) to 47 (1978) areas.

Fig. 5 AVERAGE NUMBER OF REPORTED RUBELLA CASES IN MASSACHUSETTS, NEW YORK CITY, AND ILLINOIS, BY AGE GROUP AND SELECTED PERIODS, 1966–1977*



*3-Year Averages

Fig. 6 REPORTED RUBELLA INCIDENCE RATES IN MASSACHUSETTS, NEW YORK CITY, AND ILLINOIS, BY AGE GROUP AND SELECTED PERIODS, 1966–1977*



*3-Year Averages

Fig. 7 INCIDENCE RATES OF REPORTED RUBELLA CASES, BY AGE GROUP, UNITED STATES, 1975–1977

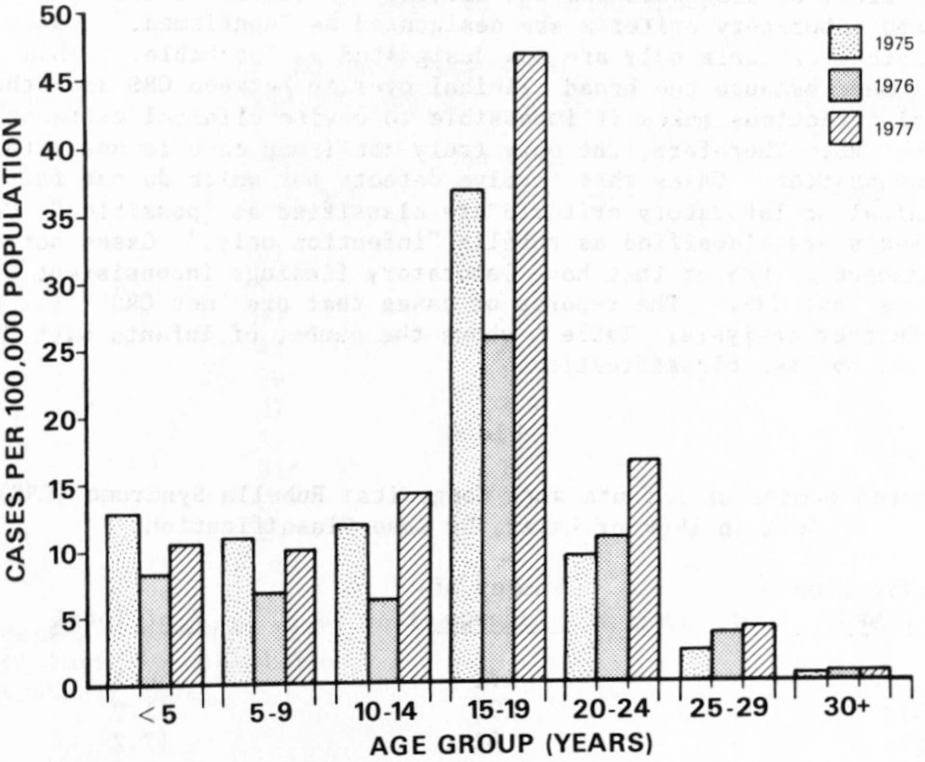
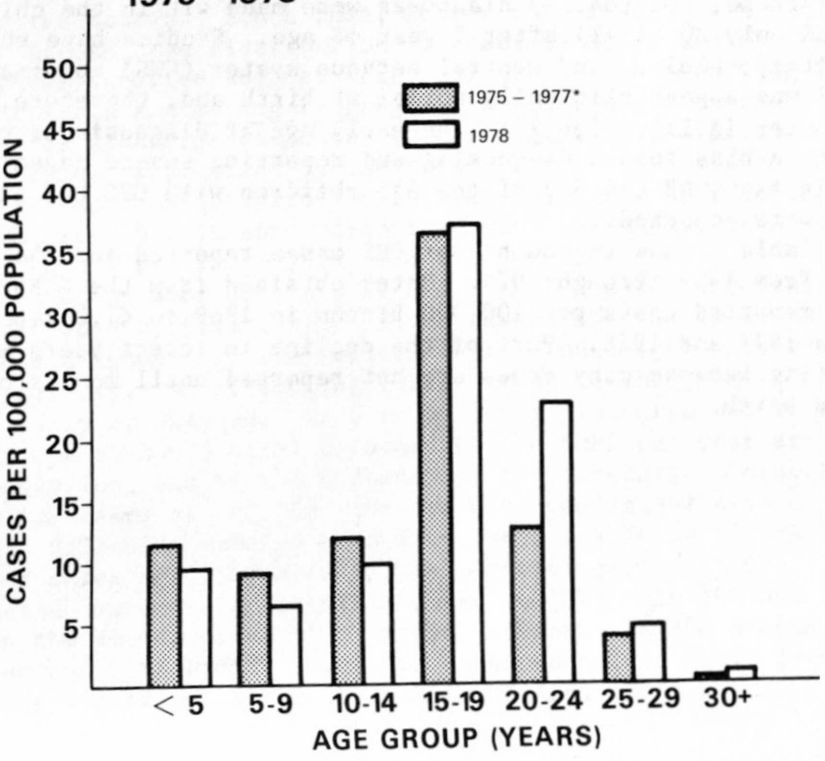


Fig. 8 INCIDENCE RATES OF REPORTED RUBELLA CASES, BY AGE GROUP, UNITED STATES, 1975–1978



*3-Year Average

made in the laboratory and clinical criteria for confirmation. Although the resulting classification is somewhat more complex, the categories more accurately reflect the certainty of diagnosis and the severity of cases. Cases which satisfy both clinical and laboratory criteria are designated as "confirmed." Cases which satisfy the clinical criteria only are now designated as "probable." This distinction was made because the broad clinical overlap between CRS and other congenital viral infections makes it impossible to devise clinical criteria which are specific for CRS. Therefore, the only truly confirmed case is one with laboratory documentation. Cases that involve defects but which do not fulfill either the clinical or laboratory criteria are classified as "possible." Cases with no recorded defects are classified as rubella "infection only." Cases not clinically diagnosed as CRS or that have laboratory findings inconsistent with CRS are classified as "not CRS." The reports of cases that are "not CRS" will be excluded from further analysis. Table 4 shows the number of infants with CRS born in 1969 or later, by case classification.

Table 4

Reported Number of Infants with Congenital Rubella Syndrome (CRS) Born in 1969 or Later, by Case Classification

Classification of Cases	Number of Infants	% of Total
Confirmed	171	36.3
Probable	193	41.0
Possible	81	17.2
Infection Only	10	2.1
Not CRS	16	3.4
TOTAL	471	100.0

Of the 455 case infants born in 1969 or later, the child's age at diagnosis was known for 314; of these, 201 (64.0%) diagnoses were made within the child's first month of life, and only 20 (6.4%) after 1 year of age. Studies have shown a high incidence of auditory, ocular, and central nervous system (CNS) abnormalities in children with CRS who appear clinically normal at birth and, therefore, are not diagnosed until later in life (5,6,7). The early age at diagnosis of cases in the NCRSR may indicate a bias toward diagnosing and reporting severe cases that are detected early. In fact, 68 (14.9%) of the 455 children with CRS had died by the time their cases were reported.

Figure 2 and Table 5 show the number of CRS cases reported and the rates of CRS by year of birth from 1969 through 1979. Rates obtained from the NCRSR show a decline from 2.7 reported cases per 100,000 births in 1969 to <1.0 reported case per 100,000 births in 1977 and 1978. Part of the decline in recent years may be due to incomplete reporting because many cases are not reported until months or even years after the child's birth.

Table 5

Cases and Rates of Congenital Rubella Syndrome, by Source of Reported Data

Year of Birth	National Congenital Rubella Syndrome Registry		Birth Defects Monitoring Program	
	Number of Cases	Rate per 10^5 Births	Number of Cases	Rate per 10^5 Births
1969	81	2.7	--	--
1970	91	3.0	42	5.0
1971	50	1.7	20	2.3
1972	42	1.4	32	3.5
1973	39	1.3	38	3.9
1974	27	0.9	29	2.7
1975	41	1.4	45	4.2
1976	31*	1.0	12	1.1
1977	27*	0.9	36	3.4
1978	18*	0.6	33**	3.4
1979	8*	--	--	--

*Reporting for recent years is incomplete, as some cases are not diagnosed until later in childhood.
**Provisional data

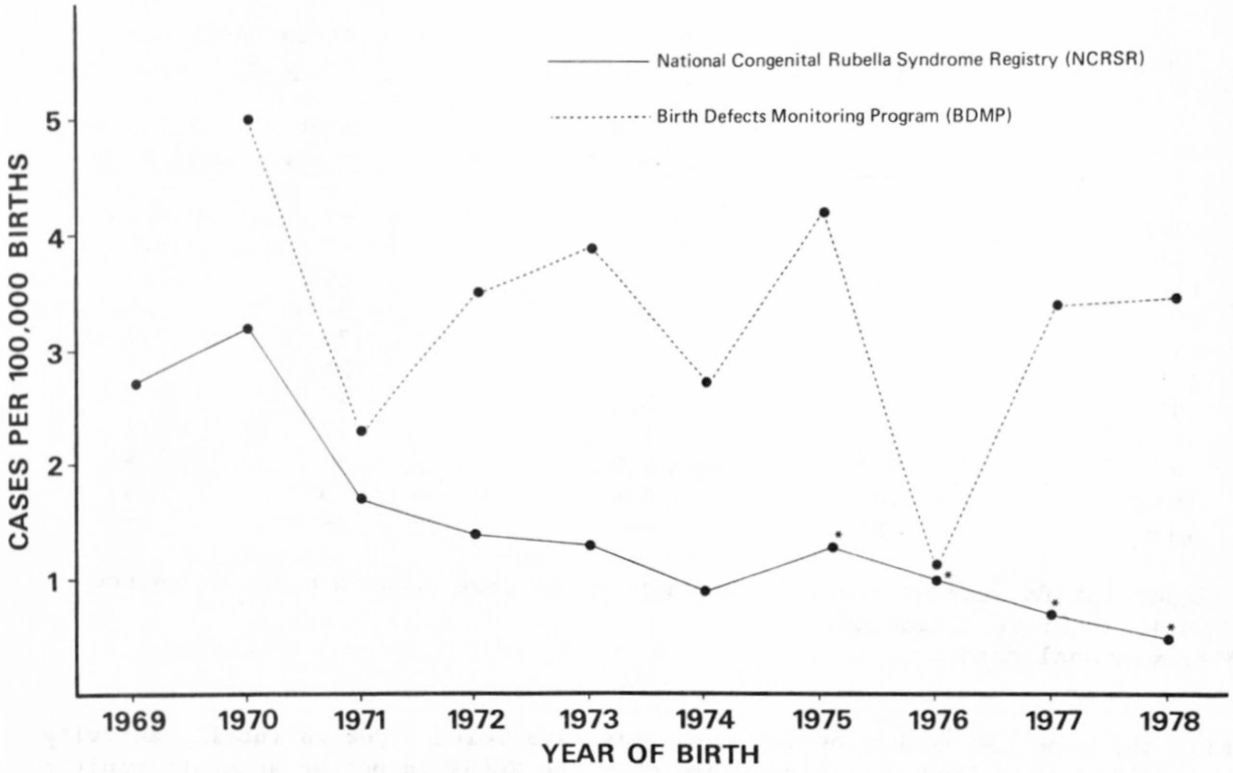
While the reported number of CRS cases has paralleled reported rubella activity fairly closely since 1969, it is possible that the NCRSR is not an accurate monitor of the magnitude of CRS for 2 reasons. First, since cases are obtained through a passive reporting system, the number of reports submitted may be a reflection of interest in the disease. The registry was begun in 1969, when rubella vaccine was licensed and interest in rubella was high. At that time, case reports were actively solicited from the states. Since then, interest in reporting has declined considerably. Second, the distribution of cases by state and the severity and early diagnosis of cases reported suggest underreporting or no reporting from many states.

2. Birth Defects Monitoring Program. The other major source of CRS data, the BDMP, monitors the discharge diagnoses of approximately 1 million newborns per year in the United States (approximately one-third of all U.S. births) through the Commission on Professional Hospital Activities (8). The BDMP shows a 32.0% decrease in rates of CRS, from 5.0 infants discharged with the diagnosis of CRS per 100,000 births in 1970 to 3.4 per 100,000 in 1978 (Table 5).

CRS rates based on BDMP data are from 1.1 to 3 times higher than those based on NCRSR findings (Table 5, Figure 9). Since cases reported to the NCRSR are not limited to those diagnosed in the newborn period, one might expect to find higher rates in the registry. An offsetting factor might be the lack of control over the quality or validity of diagnoses made on hospital discharge and included in BDMP.

If the average of 30-35 cases reported to the BDMP per year are extrapolated to the entire population, and if the accuracy of the discharge diagnosis is accepted, approximately 100 cases of CRS per year are diagnosed among all neonates in the United States. Following rubella epidemics, when suspicion of CRS is highest, less than a third of cases are diagnosed in the neonatal period (5,6). In nonepidemic periods, when the awareness of possible cases is low, only 10%-30% of all CRS are ascertained in the immediate newborn period. Hence, the 100 diagnosed cases in newborns may actually represent 300-1,000 cases annually. This is at least 10 times greater than the figures obtained through the NCRSR.

Fig. 9 RATES OF CONGENITAL RUBELLA SYNDROME BY SOURCE OF REPORTED DATA, UNITED STATES, 1969–1978



*Reporting for recent years is incomplete, as some cases are not diagnosed until later in childhood.

Both BDMP and NCRSR are limited by the diagnostic accuracy of the cases reported. BDMP is more limited because the accuracy of diagnosis cannot be verified; however, BDMP represents a source of more uniformly collected data and the rates obtained are less subject to the limitations of incomplete reporting and to the fluctuation of interest in reporting than are the NCRSR rates. The number of abortions performed on women suspected to have had rubella during pregnancy and the subsequent effect on the incidence of CRS is unknown. With current data, it is not possible to determine accurately the effect of the rubella vaccination program on the rate of fetal rubella infection during nonepidemic years.

E. Rubella Susceptibility in Postpubescent Women

An indirect measure of the success of the U.S. rubella immunization campaign is the percentage of postpubertal women who are immune to rubella. In prevaccine years approximately 15% of such women were not immune (9). Out of 52,153 serum specimens from individuals 10-40 years of age that were tested by CDC between July 1971 and March 1973, 86% were found to have an HI titer of $\geq$1:10 (3). The majority of the samples came from family planning clinics from 8 areas in the United States.

The results of immunity testing from a number of family planning clinics in Philadelphia, Pennsylvania, in the period August-October 1978 are presented in Table 6. While the results are not derived from a random survey and are drawn from an urban population, they are consistent with recently published data indicating little alteration in rubella immunity in women of childbearing age (1,10,11). The available serosurvey data are consistent with the current rubella age-specific data; both indicate strongly the need to emphasize vaccination of women of childbearing age.

Table 6

Rubella Hemagglutination-Inhibition (HI) Test Results in Women in Selected Family Planning Clinics, by Age Group, August-October 1978, Philadelphia, Pennsylvania

Age Group (Years)	Number Tested	Percentage Immune*
15-19	436	83.3
20-24	523	83.2
25-29	236	88.1
30-34	60	90.0
35-39	21	81.0
40+	18	94.5
Unknown Age	266	86.1
TOTAL	1,560	84.8

*The criterion for immunity is an HI titer $\geq$ 1:10.

III. RUBELLA IMMUNIZATION

A. Vaccine Use

In the past, delivery of rubella vaccine in the United States has been aimed primarily toward preschool and elementary school children, and recommendations for vaccination in these age groups remain unchanged. The most recent recommendations of the Advisory Committee on Immunization Practices (ACIP) regarding pregnancy counseling and serologic testing make rubella vaccination of postpubertal women simpler than before (Appendix 2).

In addition to the previously recommended premarital and prenatal screening, the ACIP now recommends that educational and training institutions such as colleges, universities, and military bases, as well as hospitals and clinics, seek proof of rubella immunity in the employees or students for whom rubella immunity would be appropriate. Rigorous attempts to vaccinate susceptible women in the postpartum period are also highly recommended.

B. Surveillance of Vaccine Use

In the period June 1969-December 1978, a total of 90.7 million doses of rubella vaccine was distributed throughout the United States. In these years the percentage of children who had been vaccinated rose from 0% to 61.7% in 1- to 4-year-olds and 0% to 73.9% in 5- to 9-year-olds (Table 7). In 1978, 64.5% of children 10-14 years of age had a history of rubella vaccination.

C. Types of Vaccine

Two vaccines are now available in the United States: RA 27/3, Meruvax II* (a derivative of the RA 27/3 strain produced in human diploid cell culture), and HPV-77:DE-5, Meruvax (a derivative of the HPV-77 strain produced in duck embryo culture). Further distribution of the RA 27/3 vaccine began in February 1979.+ Distribution of the HPV-77:DE-5 vaccine has been discontinued.

In addition to the 2 vaccines currently available, 2 other rubella vaccines have been distributed in the United States in the past: HPV-77:DK-12, Rubelogen (a derivative of the HPV-77 strain produced in dog kidney cell culture), and GMK-3:RK-53, Cendevax (a derivative of the Cendehill strain produced in rabbit kidney). Neither of these vaccines is available at this time.

*Use of trade names is for identification only and does not constitute endorsement by the Public Health Service or the Department of Health, Education, and Welfare.
+The RA 27/3 strain of rubella vaccine virus is also used in the rubella-mumps (Biavax II), measles-rubella (MR-Vax II), and the measles-mumps-rubella (MR II) preparations.

D. Duration of Immunity

A number of studies have been conducted to evaluate measured by HI antibody following rubella vaccination (Ta these studies it is important to distinguish the total ab failure of seroconversion at the time of vaccination (i.e from loss of detectable antibody due to waning immunity (In studies where immediate postvaccination titers were ob rates were consistently over 96%, i.e., the rate of prima (12-17). Long-term followup ranging from 4-9 years after of HI antibody in 0%-8.5% of vaccinees who initially sero However, many of these individuals have been found to be criteria, such as neutralizing antibody, the enzyme-linke (ELISA), and cell-mediated immunity (Herrmann, unpublishe

In contrast to the above studies, 1 study recently re rate at a mean of 4.7 years after vaccination in children with a documented his of rubella vaccination at private clinics (21). Unfortunately, immediate postvaccination titers were not obtained, and it is impossible to distinguish primary from secondary vaccine failure or to know what was the cause of primary vaccine failure, if it occurred.

While some vaccinees have been shown to maintain low postvaccination HI tit or to have no evidence of persistent cellular immunity, there is no convincing evidence indicating that these individuals, or their developing fetuses, are at of clinical reinfection with viremia (see Reinfection).

E. Reinfection

Subclinical reinfection (i.e., a 4-fold or greater rise in preexisting anti titer) following challenge by wild-type rubella virus has been described after natural and vaccine-induced immunity. In studies of institutionalized childre military groups exposed to wild-type rubella, subclinical reinfection has been demonstrated in 3.5%-80% of vaccinees compared with 1.5%-3.4% of those natural immune (23-26). Reinfection of RA 27/3 vaccinees after either exposure to wil virus or rechallenge with vaccine virus is less likely than reinfection of HPV-77:DE-5 or Cendehill vaccinees (24,27).

Although rubella virus has occasionally been recovered from the pharynx of reinfected persons, the titers of virus shed were low, and the duration of exc was abbreviated (23,28). The risk that reinfected individuals will transmit v to susceptible contacts appears to be very low; however, it is not known if th risk is totally absent.

Viremia has not been demonstrated following reinfection. Clinically appare reinfection is rare, and only a few reports exist in the literature (29-32). Serologic results supporting reinfection must be interpreted cautiously (33). example, in 1 case report primary rubella infection was originally mistaken fo documented reinfection because the HI activity demonstrated in serum samples t before "reinfection" was actually caused by nonspecific inhibitors rather than antibody (32-35).

The risk to the fetus of a woman with rubella reinfection is very low, if exists at all (36-38). However, at least 9 cases have been reported of matern reinfection during pregnancy (29,32,39,40-43). One of these reports, discusse above, represents a case of primary infection mistaken for reinfection (32). other 8 instances reported, 6 of the pregnancies were carried to term and 2 we terminated. In 1 case in which pregnancy was terminated, the diagnosis of reinfection has been questioned because the patient experienced full-blown cli rubella and the first HI titer available to document prior immunity was obtai days after the onset of rash (39,44). In the other, the patient, who also had and symptoms of rubella, had detectable HI antibodies but no demonstrable neutralization antibodies prior to her "reinfection" (29). The question of cross-reacting antibodies was discussed by the authors.

Table 7

Rubella Vaccination Status of Children,
By Year and Age Group,
United States, 1970-1978

Year	Net Doses of Vaccine Distribution[1]	Ages 1-4 Years		Ages 5-9 Years		Ages 10-12 Years	
		Population[2] (1,000's)	% with Vaccine History	Population (1,000's)	% with Vaccine History	Population (1,000's)	% with Vaccine History
1970[3]	29.3	14,123	37.2	20,421	46.5	12,437	29.5
1971	8.6	14,112	51.2	19,799	63.2	12,633	47.3
1972	7.9	13,905	56.9	18,552	66.8	12,274	55.2
1973	7.8	13,874	55.6	17,904	64.9	12,198	54.1
1974	7.6	13,210	59.8	17,515	68.0	12,249	57.5
1975	7.8	12,729	61.9	17,311	70.0	11,850	60.9
1976	6.4	12,276	61.7	17,296	69.5	11,493	61.5
1977	7.7	12,071	59.4	17,080	70.5	10,911	63.5
1978	7.6	12,187	61.7	16,793	73.9	18,371[4]	64.5

[1]Biologics Surveillance Program; doses in millions

[2]U.S. Immunization Surveys, 1970-1978

[3]Doses distributed from June 1969 through December 1970

[4]Age group 10-14 years

Table 8

Studies Evaluating Serologic Persistence of Rubella Vaccine-induced Immunity

Study (Reference No.)	Type of Vaccine	No. Vaccinated	% Seroconverting Initially	Years After Vaccination	No. Followed Up	% Seronegative
Balfour (21)	HPV-77:DE-5*	Not known		mean 4.7 (range 0.3-9)	159	36.5
Herrmann (12)	HPV-77:DE-5	1,699	97.5	4	1,241	1.8
	HPV-77:DK-12	1,742	99.9	4	1,322	0.0
	Cendehill	1,712	99.8	4	1,269	0.4
Horstmann (18)	HPV-77:DE-5	835	97.6	3-5	342	8.5
Just (14)	Cendehill			9	240	0.8
MacDonald (15)	Cendehill	200	98.5	6-8	55	0.0
	RA 27/3	96	100.0	5-6	17	0.0
Schiff (16)	Cendehill	626	98.8	7.5	204	8.0
	HPV-77:DK-12	632	99.1	7.5	216	0.5
Weibel (20)	HPV-77:DE	265	96.6	6-7.5	64	7.8
	HPV-77:DE*			6-7.5	153	2.0

*Includes both monovalent and combinations of measles, mumps, and rubella antigens

Of the 6 pregnancies carried to term, 3 resulted in normal-appearing, uninfected infants; 1 resulted in a healthy, 1760-g infant with rubella-specific IgM antibody (the authors of this case report acknowledge that primary infection could not be ruled out); 1 resulted in a normal-appearing infant with a positive pharyngeal rubella virus isolate at birth (but no detectable IgM antibody until 7 weeks of age); and 1 resulted in a congenitally malformed infant (40-43). In the last 2 cases, as in 1 case above, rubella HI activity but no neutralizing antibody was demonstrated in the mothers' serum samples prior to "reinfection."

While none of the reports definitively document reinfection, the 3 HI positive and neutralizing antibody negative cases are of interest. Although individuals vaccinated with HPV-77:DE-5 may be more likely to be deficient in neutralizing antibody and positive for HI antibody than those naturally infected or vaccinated with the RA 27/3 strain of rubella vaccine virus, none of the reported cases involved previously vaccinated individuals (45).

F. Side Effects

As would be expected from experience with other live-virus vaccines, rubella vaccine can occasionally cause rubella-like symptoms in recipients. Of particular concern have been adverse reactions involving joints (46-50). The onset of symptoms usually occurs from 7-21 days after vaccination when the vaccine virus has had time to multiply within the body. Usually symptoms are not incapacitating, although the severity ranges from morning stiffness to arthritis with joint effusions. Frank arthritis has been reported in a small percentage of susceptible vaccinees in large-scale field trials (37,51). The symptoms, which most commonly occur in the fingers, knees, hands, and wrists, usually resolve within a few days. Uncommonly, symptoms recur; they have been known to recur or persist as long as 8 years later (49,52-54). Recurrences are most often intermittent and have not progressed to permanent deformity.

The pathogenesis of rubella-associated arthropathy is poorly understood. Vaccine virus has been isolated 3-4 months after vaccination from effusions of at least 3 children with persistent symptoms (55). The results of 1 study showed depression of cell-mediated immunity to rubella virus in subjects with arthritis associated with rubella vaccination (56).

The frequency of joint symptoms varies with the age, sex, and immune status of the recipient, as well as with the type of vaccine used. As would be expected, vaccine recipients who are immune to rubella at the time of vaccination are not at increased risk of arthritis or arthalgia (46,49,57). Susceptible postpubertal women recipients are at the highest risk of joint symptoms; studies have shown that 23%-58% of this group will experience joint symptoms compared with only 2.5%-10% of children (37,46-49).

All rubella vaccines have been associated with joint symptoms, but comparative surveys indicate that HPV-77:DK-12 vaccine was more often the cause of joint complaints (51). This vaccine was voluntarily withdrawn from distribution in 1973.

Two syndromes characterized by pain and/or paresthesia in the extremities have been described following rubella vaccination (58-59). In 1 syndrome, referred to as the "arm syndrome," affected persons are typically awakened from a sound sleep by paresthesia in the arm and hand. The latent interval ranges from 10-62 days with a mean of 39 days. The symptoms last from 30 seconds to 1 hour and may occur from 1-6 times per night.

In the "catcher's crouch" syndrome, the symptoms which begin from 29-70 days (mean of 45 days) after vaccination are pain behind the knee and inability to fully extend the knee. Symptoms are worst upon getting up in the morning, and they diminish during the day. The mean interval between vaccination and onset is about 40 days; intervals of 7-99 days have been reported. Usually symptoms last from 1-5 weeks.

Recurrences have been reported over long periods for both the arm and the catcher's crouch syndromes, but particularly for the latter (60,61). Joint symptoms are usually absent with the arm syndrome, but slight synovial thickening, joint tenderness, and/or swelling have been reported in the catcher's crouch syndrome (61). Decreased nerve-conduction velocities have been demonstrated with both syndromes. The observed rate of these syndromes has been estimated roughly to be 22.0 cases/10,000 doses of HPV-77:DK-12 and 1.0 case/10,000 doses of HPV-77:DE-5 (58).

Although the RA 27/3 vaccine induces higher antibody titers than either the HPV-77:DE-5 or Cendehill vaccines, it is no more likely to cause vaccine-associated reactions (37). The vaccine has not been associated with clinically important reactions: rash may occur in 10%, fever in 4%, and lymph node enlargement in 21% of susceptible vaccinees. Joint involvement occurs infrequently and usually is not disabling. As with other rubella vaccines, older women are more likely to experience joint symptoms; however, recurrent disabling problems have not been reported.

G. Shedding and Communicability

Rubella vaccine viruses can frequently be recovered from the respiratory secretions of vaccinees for up to 28 days after vaccination (37,62). However, the virus is secreted in low titers and has not been shown to be communicable (63-69). Although there are a few case reports of contact seroconversion, contact with the wild virus or a laboratory error could not be ruled out (70-73). In addition, it is usually difficult to establish that an isolated event temporally associated with vaccination is, in fact, vaccine-associated.

Considering the importance of protecting susceptible pregnant women from exposure to and possible infection with natural rubella and the large number of studies documenting the lack of communicability of the vaccine virus strains, susceptible children living in the presence of a pregnant woman should be vaccinated. Also, even though rubella virus may be excreted in the mother's milk, there appears to be no contraindication for vaccinating a susceptible mother in the immediate postpartum period (i.e., before discharge from the hospital) if she plans to breast-feed her infant (74-76).

H. Rubella Vaccine in Pregnancy

With increasing emphasis being given to the vaccination of women of childbearing age, questions surrounding the risks of the vaccine for the developing fetus become more important. Clearly, rubella vaccine virus can cross the placenta and infect the fetus during the early stages of development (77); however, the frequency with which vaccine virus infects the fetus is difficult to estimate. A CDC review reported that 21% of women known to be susceptible at the time of vaccination and who chose abortion had culture-positive abortion specimens (includes placenta, decidua, and fetal tissue) (77). This figure is similar to the 25% reported in an earlier study (36). In the latter study, however, the virus was isolated from only 1 of 24 fetal specimens.

The Immunization Division, CDC, has been collecting information on infants born to susceptible women who were inadvertently vaccinated either shortly before conception or during the first trimester of pregnancy (3,77,78). Information is now available on 84 such infants. All were free of obvious congenital malformations at the time of birth; however, 2 had laboratory evidence of fetal infection: 1 with a rubella-specific IgM titer of $\geq$1:4 and 1 with a persistently elevated IgG level. These laboratory results indicate that subclinical fetal infection did occur following maternal vaccination, but simultaneous maternal exposure to natural rubella cannot be ruled out. These 2 children, observed for 38 months and 22 months, respectively, continue to have no apparent clinical abnormalities. A detailed report will appear in the Journal of Pediatrics in 1980 (Hayden, personal communication).

By extrapolating from the binomial distribution based on these 84 instances in which no malformations have been observed, we find that the maximum risk of a congenital malformation occurring in these circumstances is no greater than 5% (95% confidence limits), as contrasted with a risk of at least 20% from natural rubella infection (79). This risk is also similar to the 5%-7% risk that any pregnancy will result in a congenitally malformed infant simply by chance (80). For those women of unknown immune status, the maximum risk due to the vaccine is less than 1% ([10%-15% susceptibility rate]x[≤5% risk of malformation]). Thus, while the likelihood of recovering vaccine virus from aborted material is substantial, the risk of congenital malformations occurring if the pregnancy is carried to term appears to be low.

CDC has received no reports of rubella cases that have occurred in recipients of the new RA 27/3 strain of rubella vaccine virus, but available data suggest that this vaccine strain is no more teratogenic than any of the other rubella vaccine strains (81). Examination of the products of conception from 12 seronegative pregnant women who had been vaccinated with the RA 27/3 vaccine before their abortions has failed to reveal virus (82,83).

The maximum risk of congenital malformations has decreased as the reported instances of vaccine-associated complications during pregnancy have increased (77,78). Although available data are encouraging, definite conclusions regarding the risk of rubella vaccine to the fetus still cannot be drawn. Counseling regarding the advisability of abortion in this situation must be individualized. The Immunization Division continues to collect such data and encourages the reporting of all such cases so that the risks involved may be more accurately characterized. Personnel are available to receive reports and to discuss and update the data (phone: 404-329-3745).

Because of the uncertainties that still exist, women known to be pregnant should not be vaccinated, and women of childbearing age should avoid conception for 3 months after vaccination. In view of the importance of protecting this age group against rubella, the following precautions should be taken in a rubella immunization program: simply ask women if they are pregnant before vaccination, exclude those who are, and explain the theoretical risks to the others. When practical, serologic testing of potential female vaccinees of childbearing age may be undertaken to show susceptibility to rubella, but should not interfere with the effective vaccination of these individuals.

VI. SPECIAL STUDIES

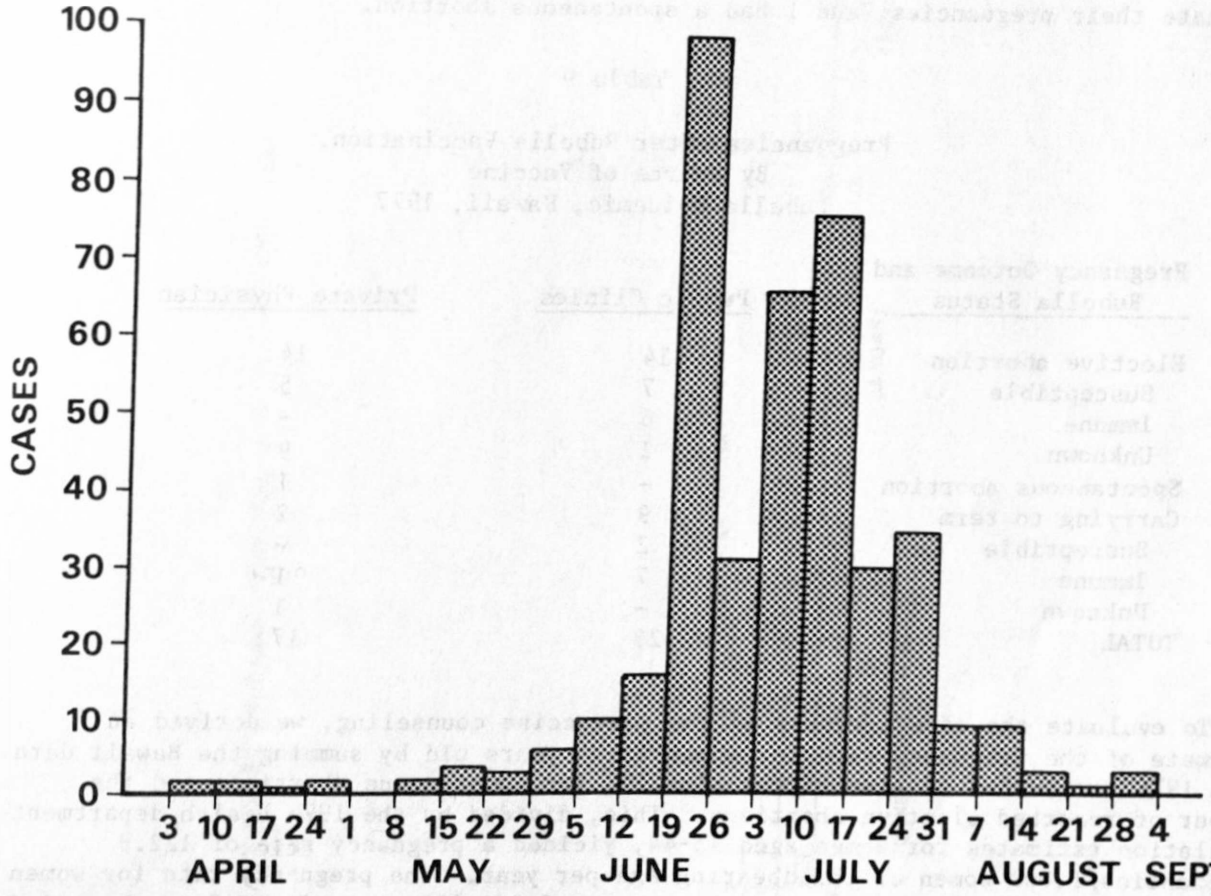
A. Rubella Outbreak in Hawaii

Between April 1 and August 31, 1977, a total of 429 cases of rubella were reported to the Hawaii State Department of Health. Dates of onset peaked the week of June 19-26, followed by a second broader peak during the weeks of July 3-17 (Figure 10). The highest age-specific attack rates occurred in 15- to 30-year-old persons with almost total sparing of school-aged children.

Because the dates of onset were suggestive of a common source of exposure and because over 50% of the patients gave a history of attendance at a specific discotheque as their only large-group exposure, a case-control study was undertaken in which persons aged 18-30 years with onset of rubella in the week of June 19-26 were matched with persons without a history of disease for age, sex, and area of residence.

This case-control study showed that 58% of the persons with rubella had attended the discotheque in the 2 weeks from May 27 to June 10, while only 16% of the matched controls had attended. In 5 pairs the control only had attended, whereas in 26 pairs the person with rubella had attended the discotheque and the control had not ($x^2 = 12.9$, $p<.001$, McNemar Test).

Fig. 10 RUBELLA CASES, BY DATE OF ONSET, HAWAII, APRIL 13—SEPTEMBER 4, 1977



In an effort to locate the source of transmission, investigators contacted the employees of the disco, as well as the bands who played there. Three members of one 11-member band gave a history of rash illness. The guitar player was the first to become ill, on April 7; his illness was confirmed serologically as rubella. Next, the drummer became ill on approximately May 15, and the piano player began having a mild rash illness on June 4. The rashes lasted only 1 or 2 days and were not accompanied by fever, cough, coryza, conjunctivitis, or lymphadenopathy. All 3 men continued to play in the band throughout the course of their illnesses and sang as well as played instruments.

The implicated discotheque was often very crowded. Fire regulations rated its maximum capacity at 300; however, the employees estimated attendance on weekend nights at 800 or more persons in the late evening. The band played in the center, and a dance floor was on both sides.

A total of 20,816 persons attended mass vaccination clinics between June 23, 1977, and September 2, 1977. Of these, 12,426 (59.7%) were women of childbearing age. A total of 6,523 women between the ages of 15 and 44 received rubella vaccine at the clinics after a blood specimen was obtained and 5,903 other women had blood drawn for analysis of rubella antibodies but were not vaccinated because they were not using effective means of preventing pregnancy (i.e., oral contraception, intrauterine device, diaphragm plus contraceptive jelly, or foam plus condom). The other 8,390 persons were men, children, and women outside the childbearing age or surgically sterilized. A total of 7,537 HI tests were performed on blood specimens obtained from women seen in the clinics--the contacts of rubella patients and pregnant women. The overall susceptibility rate was 36.9%, much higher than the 10%-15% susceptibility rates seen in the U.S. mainland population.

From the 6,523 women of childbearing age vaccinated at the mass clinics, 23 pregnancies have been reported, for a rate of 3.5 pregnancies/1,000 women vaccinated (Table 9). An additional 17 pregnancies have been reported of women vaccinated by private physicians, but the rate for this group could not be determined because the total number of women immunized is unknown. A total of 28 (68%) women elected to terminate their pregnancies, and 1 had a spontaneous abortion.

Table 9

Pregnancies After Rubella Vaccination,
By Source of Vaccine
Rubella Epidemic, Hawaii, 1977

Pregnancy Outcome and Rubella Status	Public Clinics	Private Physician
Elective abortion	14	14
Susceptible	7	5
Immune	6	-
Unknown	1	9
Spontaneous abortion	-	1
Carrying to term	9	2
Susceptible	2	-
Immune	7	1
Unknown	-	1
TOTAL	23	17

To evaluate the effectiveness of the prevaccine counseling, we derived an estimate of the pregnancy rate for women 15-44 years old by summing the Hawaii data from 1976 for number of live births plus 10% for spontaneous abortions and the number of reported elective abortions. This, divided by the 1975 health department population estimates for women aged 15-44, yielded a pregnancy rate of 122.8 pregnancies/1,000 women of childbearing age per year. The pregnancy rate for women vaccinated in the mass vaccination clinics was 3.5/1,000 women for a 3-month period, or 14.0/1,000 women per year. Therefore, the screening for birth control and counseling regarding the importance of continued proper birth control was effective in selecting women who were not going to become pregnant in the 3 months after vaccination. The efficacy of screening and counseling was 88.6% when efficacy is calculated according to the following formula:

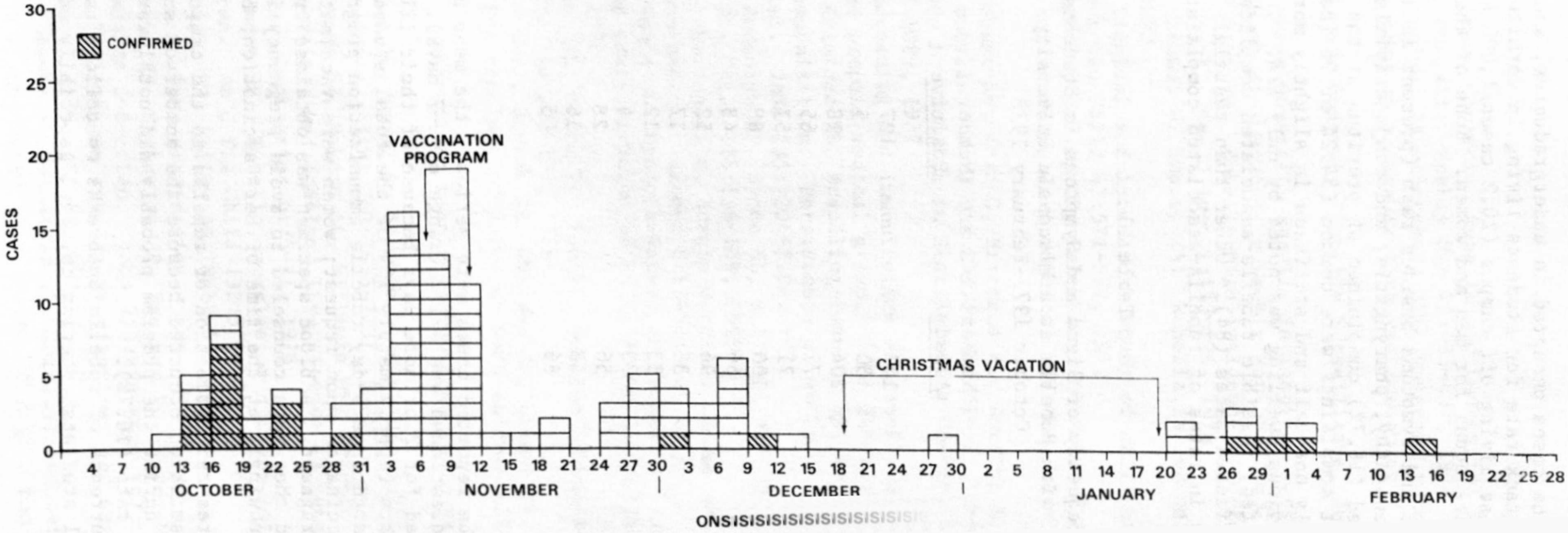
$$\frac{\text{(Annual pregnancy rate in unscreened - annual pregnancy rate in screened)}}{\text{(Annual pregnancy rate in unscreened)}} \times 100\%$$

In addition to the rubella vaccinees who became pregnant, 12 women who had had recently diagnosed cases of rubella were reported to have become pregnant. Eleven of these women elected to terminate their pregnancies. The other woman, who had serologically confirmed rubella at 3-1/2 months' gestation, continued her pregnancy to term and delivered a normal-appearing infant.

B. Rubella in Wisconsin--An Outbreak on a College Campus

Between October 12, 1977, and February 14, 1978, a total of 107 cases of rubella were reported to the health director of a university in Wisconsin (Figure 11). The case definition used in the investigation was rash plus fever and/or lymphadenopathy. Eighteen cases were confirmed as rubella by a 4-fold rise in HI antibody titers and/or isolation of the virus from pharyngeal specimens. In 4 other cases rubella-specific IgM antibody was elevated.

Fig. 11 RUBELLA CASES AT A UNIVERSITY, BY ONSET OF RASH, WISCONSIN, OCTOBER 1977–FEBRUARY 1978



One hundred five of the cases occurred in undergraduates, and all 4 classes were equally affected. The attack rate for students living in dormitories was nearly 3 times higher than for those living off campus (20.2 cases/1,000 students versus 7.0/1,000). The rates were equal for men and women. None of the affected women were pregnant.

The most common signs and symptoms besides rash (present in all cases by definition) were lymphadenopathy, pharyngitis, and conjunctivitis (Table 10). Five of 30 students interviewed (16.7%) complained of pruritus at the onset of their rash. As expected, joint complaints were common (54.2% of 96 individuals). Pain was noted in approximately one-half and stiffness in slightly more than one-third of affected individuals; obvious swelling was noted by only 12%. Interestingly, testalgia--a newly reported, possible rubella-associated complication--was reported by 5 (7.6%) of the 66 affected males (84). Other than testalgia, there were no sex-specific differences in rates of rubella-associated complaints.

Table 10

Frequency of Signs and Symptoms in Students with Rubella at a Wisconsin University October 1977-February 1978

Sign/Symptom	Number Asked	Number Positive	Percent
Rash	107	107	100.0
Pruritis	30	5	16.7
Lymphadenopathy	104	98	94.2
Pharyngitis	77	65	84.4
Conjunctivitis	71	57	80.3
Temperature ≥100°F	100	68	68.0
Headache	66	43	65.2
Joint Complaint	96	52	54.2
Pain	33	17	51.5
Stiffness	33	12	36.4
Swelling	33	4	12.1
Coryza	56	28	50.1
Cough	48	16	33.3
Testalgia	66	5	7.6

Although none of the reported cases were serious, the mean number of class days missed by 45 students questioned was 4-1/2 (range of 1-7 days). Over 90% of these students remained in bed for 2 or more days because of their illness.

Almost 1,200 students (approximately 10% of the total student body), including 526 women, were vaccinated in a 5-day rubella immunization program prompted by the outbreak. Men were vaccinated upon request; women were vaccinated only if they stated they were not pregnant. A blood specimen was obtained from all women just before vaccination, and they were counseled to avoid pregnancy for 3 months. One woman was pregnant unknowingly at the time of her vaccination; her full-term infant was normal at birth.

Figure 11 illustrates reintroduction of rubella to the campus after a 1-month vacation period. Transmission occurred because the number of susceptible individuals vaccinated during the program probably did not lower significantly the overall susceptibility rate (16.7%).

The continuing occurrence of rubella outbreaks on college campuses supports the need to insure that all students entering college, especially women, are immune to rubella.

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PREVIOUS CRITERIA FOR CLASSIFICATION OF
CONGENITAL RUBELLA SYNDROME (CRS) CASES

I. CRS Confirmed
Clinical--any 2 complications listed in A or 1 from A and 1 from B

A. Cataracts, loss of hearing, congenital heart disease (patent ductus arteriosus, peripheral pulmonic stenosis, atrial septal defect, or ventricular septal defect), congenital glaucoma, radiolucent bone lesions

B. Purpura, hepatosplenomegaly, neonatal jaundice, microcephaly, mental retardation

Laboratory--isolation of rubella virus during the neonatal period from any child with the appropriate clinical signs, and appropriate serologic evidence of congenital rubella infection--significant titer of hemagglutination inhibition antibody to rubella virus in serum collected from infants between 6 and 11 months of age, or increased IgM antibodies to rubella virus in the neonatal period

II. CRS Compatible
Cases which do not fulfill the above criteria for a probable case, but are compatible with CRS

I. Not CRS
Cases which are clearly not CRS

PROPOSED CRITERIA FOR CLASSIFICATION OF
CONGENITAL RUBELLA SYNDROME (CRS) CASES

I. CRS Confirmed
Defects present and 1 or more of the following:
Rubella virus idolated
Rubella-specific IgM present
Rubella hemagglutination-inhibition (HI) titer in the infant $\geq$3 months of age persisting above and beyond that expected from passive transfer of maternal antibody (i.e., rubella HI titer in the infant which does not fall off at the expected rate of one 2-fold dilution per month)

. CRS Probable
Clinical documentation with lab data insufficient for confirmation
Any 2 complications listed in A or 1 from A and 1 from B

A. Cataracts/congenital glaucoma (either or both count as 1), congenital heart disease, loss of hearing, pigmentary retinopathy

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

. CRS Possible
Compatible clinical findings which do not fulfill the above criteria for a probable case

. Congenital Rubella Infection Only
No defects present
and
Lab evidence of infection (see criteria for confirmed category)

. Not CRS
1 or more of any of the following inconsistent lab findings in child without evidence of an immunodeficiency disease
Rubella HI titer absent in a child $\leq$24 months
Rubella HI titer absent in mother
Rubella HI titer decline in an infant $\geq$3 months of age consistent with the normal decline of passively transferred maternal antibody after birth (the expected rate of decline of maternal antibodies is one 2-fold dilution per month)

Recommendation of the Public Health Service
Advisory Committee on Immunization Practices

JANUARY 1979
Reprinted from MMWR
27:451-454, 459, 1978

RUBELLA VACCINE

Changes in the ACIP recommendation for the use of rubella vaccine focus on more effective delivery of the vaccine to older individuals and, in particular, to females in the childbearing age group. All comments related to the vaccine and its use pertain both to the HPV-77 DE5 (Meruvax) and to the RA 27/3 (Meruvax II) strains of vaccine virus. The RA 27/3 vaccine—like the HPV-77 DE5 vaccine—is licensed for subcutaneous administration only and is expected to be available in January 1979.

INTRODUCTION

Rubella is a common childhood rash disease that is often overlooked or misdiagnosed. Signs and symptoms vary. The most common features—postauricular and suboccipital lymphadenopathy, arthralgia, and transient erythematous rash with low fever—may not be recognized as rubella. Moreover, subclinical infection occurs frequently. Transient polyarthralgia and polyarthritis sometimes accompany or follow rubella illness. This occurs in women in particular, but it is also seen in men and in children. Central nervous system disorders and thrombocytopenia have been reported, but they are rare.

By far the most important consequences of rubella are the fetal anomalies that frequently result from rubella infection in early pregnancy, especially in the first trimester. Preventing infection of the fetus and consequent congenital rubella syndrome is a major objective of rubella immunization programs.

Postinfection immunity appears to be long-lasting. However, as with other viral diseases, re-exposure to natural rubella occasionally results in reinfection without clinical illness. The only reliable evidence of rubella immunity is specific antibody, best determined by hemagglutination-inhibition (HI) antibody technique. Laboratories that regularly perform this test are generally the most reliable because of better standardization of reagents and procedures.

Before rubella vaccine was available, most cases of rubella occurred in school-age children. Now, most cases are in adolescents and young adults. In 1977, 70% of cases occurred in those 15 years of age and older. Of persons in these age groups, 10%-20% are susceptible. Since licensure of rubella vaccine in 1969, the incidence of reported rubella in adolescents and young adults has not decreased appreciably because vaccine was primarily used for preschoolers and elementary school children. Through 1977, more than 80 million doses of live attenuated rubella virus vaccine were distributed in the United States. Despite the considerable vaccination effort in young children, outbreaks of rubella continue to be reported in junior and senior high schools, colleges, the military, and places of employment—most notably hospitals.

LIVE RUBELLA VIRUS VACCINE

Live rubella virus vaccine* available in the United States is prepared either in duck embryo cell culture or human diploid cell culture. It is produced in monovalent (rubella only) form and in combinations: measles-rubella (MR) and measles-mumps-rubella (MMR) vaccines. MMR is encouraged for use in routine infant-child vaccination programs. In all situations in which rubella vaccine is to be used, consideration should be given to using a combination vaccine if recipients are likely to be susceptible to measles and/or mumps as well as to rubella.

A single dose of rubella vaccine at 12 months of age or older induces antibodies in approximately 95% of susceptible persons. Although antibody titers are generally lower

*Official name: Rubella Virus Vaccine, Live

than those following rubella infection, vaccine-induced immunity protects against clinical illness from natural exposure. Antibody levels have declined little during the more than 9 years of follow-up of children who were among the first to receive the vaccine. Long-term, even life-long, protection against both clinical rubella and subclinical viremia is expected.

Rubella reinfection without illness can occur in persons with low levels of antibody whether the antibodies resulted from vaccination or from natural rubella. Reinfection, however, does not cause detectable viremia or significant pharyngeal excretion of virus and thus poses no recognized risk to susceptible contacts. Further study is needed to evaluate the clinical and epidemiologic significance of reinfection, but the apparent absence of viremia suggests that immune females reinfected during pregnancy would be unlikely to infect their fetuses.

VACCINE USAGE

General Recommendations

Rubella vaccine is recommended for all children, many adolescents, and some adults, particularly females, unless it is otherwise contraindicated. Vaccinating children protects them against rubella and prevents their subsequently spreading it. Vaccinating susceptible postpubertal females confers individual protection against rubella-induced fetal injury. Vaccinating adolescent or adult males and females in population groups such as those in colleges, places of employment, or military bases, protects them against rubella and reduces the chance of epidemics in partially immune groups.

Dosage: A single dose of vaccine in the volume specified by the manufacturer should be administered subcutaneously.

Individuals at Risk

Live rubella virus vaccine is recommended for all children when 12 months of age or older. It should not be administered to younger infants because persisting maternal antibodies may interfere with seroconversion. When the rubella vaccine is part of a combination vaccine that includes the measles antigen, it should be administered to children about 15 months of age or older to achieve the maximum rate of measles seroconversion. Children who have not received rubella vaccine at the optimum age should be vaccinated promptly. Because a history of rubella is not a reliable indicator of immunity, all children for whom vaccine is not contraindicated should be vaccinated.

Increased emphasis should be placed on vaccinating unimmunized prepubertal girls and susceptible adolescent and adult females in the childbearing age group. Because of the theoretical risk to the fetus, females of childbearing age should receive vaccine only if they are not pregnant and understand that they should not become pregnant for 3 months after vaccination. In view of the importance of protecting this age group against rubella, asking females if they are pregnant, excluding those who are, and explaining the theoretical risks to the others are reasonable precautions in a rubella immunization program. When practical, serologic testing of potential vaccinees in the childbearing age group may be undertaken to show susceptibility to rubella.

Educational and training institutions such as colleges, universities, and military bases should seek proof of rubella immunity (a positive serologic test or documentation of previous rubella vaccination) from all female students and employees in the childbearing age. Non-pregnant females who lack proof of immunity should be vaccinated unless contraindications exist.

When reliable laboratory services are available, routine premarital serology for rubella immunity would enhance efforts to identify susceptible females before pregnancy. Prenatal or ante partum screening for rubella susceptibility should be undertaken and vaccine administered in the immediate postpartum period—*prior* to discharge. Previous administra-

tion of anti-Rho (D) immune globulin (human) or blood products is not a contraindication to vaccination; however, 6- to 8-week postvaccination serologic testing should be done on those who have received the globulin or blood products to ascertain that seroconversion has occurred. Obtaining laboratory evidence of seroconversion in other vaccinees is not necessary.

In order to protect susceptible female patients and female employees, persons working in hospitals and clinics who might contract rubella from infected patients or who, if infected, might transmit rubella to pregnant patients should be immune to rubella.

Individuals Exposed to Disease

Use of vaccine following exposure: There is no evidence that live rubella virus vaccine given after exposure will prevent illness or that vaccinating an individual incubating rubella is harmful. Since a single exposure may not result in infection and postexposure vaccination would protect an individual in the event of future exposure, vaccination is recommended unless otherwise contraindicated.

Use of immune serum globulin following exposure: Immune serum globulin (ISG) given after exposure to rubella will not prevent infection or viremia, but it may modify or suppress symptoms. The routine use of ISG for postexposure prophylaxis of rubella in early pregnancy is not recommended. (Infants with congenital rubella have been born to women who were given ISG shortly after exposure.) The only time when ISG might be used is when rubella occurs in a pregnant woman who would not consider termination of pregnancy under any circumstances. Serologic testing for rubella immunity is useful if an exposure in early pregnancy is suspected.

SIDE EFFECTS AND ADVERSE REACTIONS

Vaccine side effects such as rash and lymphadenopathy occasionally occur in children. Joint pain, usually of the small peripheral joints, has been noted in up to 40% of vaccinees in large-scale field trials, although frank arthritis is reported in fewer than 1%. Arthralgia and transient arthritis occur more frequently and tend to be more severe in susceptible women than in children. When joint symptoms or non-joint-associated pain and paresthesia do occur, they generally begin 2-10 weeks after immunization, persist for 1-3 days, and rarely recur. The persistent arthritic symptoms that have occasionally been described probably represent coincidental disease rather than a vaccine complication. Transient peripheral neuritic complaints such as paresthesia and pain in the hands and feet have also occurred but are very uncommon.

Some vaccinees intermittently shed small amounts of virus from the pharynx 7-28 days after vaccination. However, studies of more than 1,200 susceptible household contacts have yielded no evidence that vaccine virus has been transmitted. These data strongly suggest that vaccinating susceptible children whose mothers or other household contacts are pregnant does not present a risk.

Although vaccine is safe and effective for all ages over 12 months, its safety for the developing fetus is not fully known. Thus, rubella vaccine is **NOT** suitable for pregnant women because of the theoretical risk of fetal abnormality caused by the vaccine virus, which does cross the placenta. Although no recognizable malformations attributable to rubella have been seen in infants born to more than 60 susceptible women who inadvertently received rubella vaccine during early pregnancy and continued their pregnancies to term, the theoretical risk remains.

PRECAUTIONS AND CONTRAINDICATIONS

Pregnancy

Pregnant women should not be given rubella vaccine. If a pregnant woman is inadvertently vaccinated or if she becomes pregnant within 3 months of vaccination, she should be counseled on the theoretical risks to the fetus.

Febrile Illness

Persons with febrile illness should not be vaccinated until they have recovered. Minor illnesses such as upper respiratory infections, however, do not preclude vaccination.

Allergies

Live rubella virus vaccine is produced in duck embryo cell culture or in human diploid cell culture. It has not been reported to be associated with allergic reactions and can be given to all who need it, including persons with allergies to eggs, ducks, and feathers. Live rubella virus vaccine does not contain penicillin. Some vaccines do contain trace amounts of other antibiotics, however, to which patients may be allergic. Those administering vaccines should review the label information carefully before deciding whether patients with known allergies to such antibiotics can be vaccinated safely.

Altered Immunity

Replication of the rubella vaccine virus may be potentiated in patients with immune deficiency diseases and by the suppressed immune responses that occur with leukemia, lymphoma, or generalized malignancy or with therapy with corticosteroids, alkylating drugs, antimetabolites, or radiation. Patients with such conditions should not be given live rubella virus vaccine.

Simultaneous Administration of Certain Live Virus Vaccines

See "General Recommendations on Immunization," MMWR 25:349-350, 355, 1976.

OUTBREAK MANAGEMENT

To prevent the spread of rubella in outbreaks, susceptibles at risk should be vaccinated promptly. Women at risk of exposure who are not aware of being pregnant and agree to prevent conception for 3 months should be vaccinated. Although prevaccination serologic testing is not necessary, it may be useful to collect a blood specimen at the time of vaccination. Later, it can be tested if the woman had been pregnant at the time of vaccination or should become pregnant in the next 3 months.

SURVEILLANCE

Accurate diagnosis and reporting of rubella, congenital rubella syndrome, and vaccine complications are of great importance in assessing the progress in rubella control. Furthermore, all cases of birth defects suspected of being related to rubella should be thoroughly investigated and reported to state health departments.

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Replaces previous recommendation on this subject, "Rubella Vaccine" (MMWR 26:385-386, 391, 1977)

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