Susceptibility to Epidemic Rubella in a College Population

J. F. FINKLEA, M.D., Dr.P.H., S. H. SANDIFER, M.D., O. M. PITTS, M.S., and J. M. RAVENEL, B.S.

RUBELLA in the United States has exhibited epidemic cycles of 5 to 7 years, the most recent epidemics having occurred in 1958 and 1964–65 (*1*). Serologic surveys have provided point estimates in time of rubella susceptibility, but serologic assessment of such susceptibility over an entire epidemic cycle has not been possible (*2–6*). Two recent epidemics of rubella among the cadet corps of the Citadel, a military college in Charleston, S.C., provided a natural experiment for measuring the susceptibility to rubella of the college freshmen from 1960 through 1966—that is, from trough to trough in one cycle of a national epidemic of the disease. An ongoing study of acute respiratory disease at the college, in which sporadic rubella was also monitored, allowed confirmation in the laboratory of the population's susceptibility. Thus, susceptibility, introductions of the disease, and epidemics could be correlated. The clinical and laboratory aspects of the 1967 epidemic have been reported elsewhere (*7*).

Materials and Methods

Setting and population at risk. The cadet corps of the Citadel at the time of the study was composed of almost 2,000 able-bodied young men, of whom 40 percent were South Carolinians while the remainder came from 45 other States and five foreign countries. School policy required that any cadet with clinical rubella be confined in the Citadel hospital, which also provided ambulatory and inpatient care for all other illnesses of the cadets. Finklea and Sandifer, attending physicians at the college since 1964, reviewed detailed hospital records from September 1960 through June 1968.

Serologic study. Before a study of influenza vaccine was undertaken at the Citadel in September 1967, serums were obtained from 103 well upperclassmen and 100 well freshmen. Hemagglutination inhibition tests for rubella were performed on these serums by the microtiter system according to the method of the National Communicable Disease Center. Twofold dilutions from 1:10 to 1:160 were used; a titer of 1:20 or greater was arbitrarily selected as evidence of immunity. Known positive and negative serums were included as controls with each battery of tests.

Results

Rubella epidemics harvested 175 susceptibles at the Citadel in 1964 and 96 in 1967. In both epidemics, rubella was widely seeded through every cadet barrack (*7*). Sporadic serologically confirmed rubella was observed in 1968 but did not occur in either 1965 or 1966. In table 1, the number of cases of rubella and the percent in each class cohort in the epidemic years 1964 and 1967 are distributed according to the year members of the class cohort entered college. The cohort that entered college in 1963 was exposed to both rubella epidemics; 11.91 percent of the

Dr. Finklea and Dr. Sandifer are associate professors of preventive medicine, Medical College of South Carolina, Charleston. Mr. Pitts is with the department of microbiology and Mr. Ravenel is a senior medical student at the college. *The work described was supported in part by General Research Support Grant FR 5420 from the Division of Research Facilities and Resources, National Institutes of Health, Public Health Service.*

cohort became ill in 1964 but only 1.83 percent in 1967, for a total of 13.74 percent over the two epidemics. As expected, no member of the 1963 cohort became ill during both epidemics. Since 0.867 of all the clinical rubella in the 1963 cohort was observed during the first epidemic, potential cases of clinical rubella in other class cohorts could be calculated by multiplying their observed rubella incidence by 1.1534, the reciprocal of 0.867.

Previous studies have shown a clinical to subclinical ratio for rubella cases of 2:1; that is, 1.5 total rubella cases occurred for each clinical case (*8–12*). Thus, the proportion of total rubella cases in the 1963 cohort was 17.87 percent in 1964 and 2.74 percent in 1967, or 20.61 percent over both epidemics.

The experience of the 1963 class cohort served as the basis for calculating the susceptibility to rubella of other class cohorts. To estimate the proportion of other class cohorts that would be susceptible, the percent of the cohort with epidemic cases was multiplied by correction factors for subclinical cases and for unharvested susceptibles.

$$\text{Proportion of original population susceptible} = \frac{\text{rubella cases}}{\text{population at risk}} \times \text{correction factor for subclinical cases} \times \text{correction factor for unharvested susceptibles,}$$

or

percent susceptible = percent with cases $\times 1.5 \times 1.1534$.

Both pre-epidemic point estimates and estimates of the 95 percent confidence intervals for susceptibility for the 1960 through 1966 class cohorts are shown in the following table:

Year class entered	Percent susceptible to rubella: Point estimates	Percent susceptible to rubella: Confidence intervals
1960	14.0	10.6–17.4
1961	13.6	10.2–17.0
1962	17.8	14.4–21.3
1963	20.6	17.2–24.1
1964	9.7	6.9–12.4
1965	8.9	6.6–11.2
1966	10.8	8.2–13.4
1967	14.0	7.2–20.8

Table 1. Distribution of cases of epidemic rubella in the epidemic years 1964 and 1967 among classes entering the Citadel, 1960–66

Year class entered	Population at risk	Cases: Number	Cases: Percent	Cases: Epidemic year
1960	396	32	8.08	1964
1961	395	31	7.85	1964
1962	475	49	10.32	1964
1963	529	63	11.91	1964
1963	381	7	1.83	1967
1964	448	25	5.58	1967
1965	584	30	5.14	1967
1966	545	34	6.24	1967

Similar estimates for the 1967 cohort were made on the basis of hemagglutination inhibition titers. In the 4 years before the large national rubella epidemic in 1964, class cohorts exhibited an increasing susceptibility to rubella until a peak of 20.6 percent was reached just before the epidemic. Although the confidence intervals for rubella susceptibility of the class cohorts before 1964 overlap, the trend toward increasing susceptibility is apparent. After the 1964 national epidemic, entering class cohorts have been less susceptible but were showing evidence of an increase in susceptibility by 1967.

The percent of postepidemic susceptibles in the class cohorts that entered the Citadel from 1960 through 1966 was also estimated by multiplying the total percent of susceptibles in a class cohort by a correction factor of 0.133 for unharvested susceptibles. This figure was derived from the experience of the 1963 cohort.

Percent of postepidemic susceptibles = preepidemic point estimates $\times 0.133$.

The resulting percentages of postepidemic susceptibles have varied little over the years, as the following list for the 1960–66 cohorts shows:

Year class entered	Percent of susceptibles
1960	1.9
1961	1.8
1962	2.4
1963	2.7
1964	1.3
1965	1.2
1966	1.4

With knowledge of the percentage of each class which was susceptible in any one year and of the class distribution of the entire cadet corps, the percentage of the entire corps which was susceptible to rubella in any one year could be calculated. Moreover, because of the clinical and laboratory monitoring of acute illnesses of the cadets, rubella challenges to the corps could be documented. Point and range estimates of the susceptibility of the entire corps and information on rubella challenges and rubella epidemics are included in table 2 by calendar year from 1964 through 1968. Before the 1964 epidemic, the point estimate of the corps' susceptibility was 16.9 percent; the range estimate was 13.5 to 20.3 percent. In the two succeeding nonepidemic years, when there was no clinical rubella challenge, the susceptibility of the corps was 4.5 percent in the first year and 6.5 percent in the second. By 1967, the susceptibility of the corps had risen to 8.4 percent, and a clinical rubella challenge consisting of three separate introductions of the disease resulted in an epidemic. In 1968, however, when the corps' susceptibility was 4.7 percent, two serologically documented clinical rubella challenges did not result in an epidemic. According to a 1968 personal communication from Dr. J. W. Rhodes, member of a group pediatric practice in Charleston, the actual challenge to the corps was probably more extensive than that which was serologically documented since in 1968 an extensive rubella outbreak occurred in several Charleston elementary schools.

The predicted estimates of the cadet corps' susceptibility were confirmed by serologic studies in September 1967. In a sample of 100 cadets from the 1967 class cohort, 14.0 percent were susceptible. This sample differed radically in susceptibility from one drawn from upperclassmen of the 1964, 1965, and 1966 cohorts, in which 2.91 percent of the cadets were susceptible (chi square, 1 degree of freedom=8.31; $0.01>P>0.001$). However, the serologically observed point estimate of the upperclassmen's susceptibility—2.91 percent with a confidence interval of 0 to 8.87 percent—did not differ significantly from the point estimate of 1.28 percent and the confidence interval of 0 to 1.92 percent derived from point estimates of the postepidemic susceptibility of each component class cohort and of the cohort composition of the sample of upperclassmen.

Table 2. Estimated percent of the cadet corps susceptible to rubella, 1964–68

Calendar year	Susceptibles		Rubella challenge	Rubella epidemic
	Point estimates	Range estimates		
1964	16.9	13.5–20.3	Yes	Yes
1965	4.5	3.7– 5.3	No	No
1966	6.5	5.0– 8.0	No	No
1967	8.4	6.4–10.4	Yes	Yes
1968	4.7	2.9– 6.6	Yes	No

Discussion

Estimates of rubella susceptibility in this report rest upon the experience during two epidemics of a cohort comprised of a single college class. The validity of this experience might be questioned. Several other investigators have previously recorded the percent of rubella susceptibles harvested in smaller populations. Sever observed that 12 percent of 160 susceptible pregnant women in the general population were harvested during the 1964 epidemic (*10*). However, this risk group, above all others, would seek to avoid contact with clinical rubella. Schiff and associates found that 54 percent of a small group of susceptible women with heavy rubella exposure were harvested (*8*).

Among military recruits at Fort Ord, Peczenik observed a harvest of rubella of almost 100 percent during the first 8 weeks of training (*13*). Likewise, a harvest of 100 percent was observed by Sever and associates during a 1963 epidemic on the Pribilof Islands (*9*) and by Meyer in an Arkansas children's home (*11*). Within this context of harvests from 12 to 100 percent, the estimate of 86.7 percent in the semi-closed population of the Citadel seemed reasonable.

Point estimates of the susceptibility of class cohorts at the Citadel ranged from a high of 20.6 percent just before the 1964 national epidemic to a low of 9.0 percent just after it. Thus, a twofold difference in susceptibility to rubella was noted at the extremes of the epidemic cycle. The susceptibility of the 1960 and 1967 class

cohorts midway through different epidemic cycles was in both instances 14 percent. There has been no evidence of sex differences in susceptibility to rubella. Thus, the estimates of susceptibility for the Citadel cohorts during an epidemic cycle mirror the susceptibility of cohorts of females entering the prime childbearing years (*5, 14*). Moreover, differing point estimates for the susceptibility of females to rubella in surveys of different areas of the United States were generally bracketed by the point estimates at the extremes of the epidemic cycle noted at the Citadel (*3*).

The semi-closed college population of 2,000 at the Citadel supported the epidemic transmission of rubella virus when as small a proportion of the population as 8.4 percent was susceptible, but epidemic rubella failed to occur when the population's susceptibility was 4.7 percent. Thus, the epidemic threshold for this population probably rested between 4.7 and 8.4 percent. Epidemic thresholds would of course vary according to both the composition of the population and the intensity of the rubella challenge. Data on the epidemic threshold as well as a satisfactory serologic method for assessing rubella susceptibility and modern sampling techniques would aid college officials in making decisions about the feasibility of future rubella immunization programs. Such officials should weigh the cost of immunization against the impact of rubella on the individual student, on the student body as a group, and on the available resources for medical care.

Summary

Two rubella epidemics at the Citadel, a military college in South Carolina, provided an opportunity to assess the cadets' susceptibility to rubella from midway in the 1957–64 national epidemic cycle to 4 years after the 1964 epidemic peak. Just before the peak, 20.6 percent of an entering class cohort was found to be susceptible to the disease as compared with only 9.7 percent of the cohort that entered the college the following year. At midpoint in the epidemic cycle the susceptibility of the class cohorts was estimated to be 14.0 percent. The epidemic threshold in this semi-closed population lay between 4.7 and 8.4 percent. The estimates of susceptibility were confirmed by serologic testing.

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