

Rubella Susceptibility in Young Adults

Sharon Allen, MD, PhD, Caroline Mason, and Richard L. Holloway, PhD
Minneapolis, Minnesota

Despite widespread availability of rubella vaccine, a substantial group of young women remain at risk for delivery of infants with congenital rubella syndrome. In this study of 224 women students of childbearing age seen at a university gynecological clinic, 10.3 percent were shown serologically to have nonimmune rubella status. Of this group only five women returned for free immunization. Compliance and motivation appeared lacking. Patient history of infection or immunization was found to be unreliable; 59 percent of the sample population were uncertain of their immune status, and 32 percent showed poor understanding of rubella. Serological testing appears to be the only reliable test for detecting immune status.

Despite the widespread availability of rubella vaccine, there continues to exist a substantial susceptibility among the childbearing young adults. This susceptibility presents considerable risk both to individuals and to the public and calls for continued efforts to achieve herd immunity against rubella.

Nonimmune women are at risk for the delivery of infants with congenital rubella syndrome. Teratogenic potential of rubella infection is high; the frequency of fetal damage following first-trimester maternal infection is estimated to be more than 20 percent. The syndrome of congenital rubella may include heart malformations, eye lesions, deafness, mental retardation, purpura, splenomegaly, and meningoencephalitis.¹

From a population perspective, the incidence of rubella from 1928 to 1967 in ten selected areas of the United States shows major epidemics of rubella occurring at six- to nine-year intervals. For example, in the United States, the 1964 epidemic

resulted in approximately 30,000 stillbirths and 20,000 babies born with congenital rubella syndrome at an estimated cost of \$2 billion.² In response to these epidemics, efforts to develop a vaccine were stepped up, resulting in RA 27/3 rubella vaccine commonly used today.

Studies concerned with the possible teratogenicity of the current RA 27/3 rubella vaccine have noted no defects attributable to congenital rubella syndrome. The observed risk for congenital rubella syndrome following rubella vaccination continues to be zero.¹ The Immunization Practices Advisory Committee recommends that pregnancy remain a contraindication to rubella vaccination but that inadvertent rubella vaccination of a pregnant woman should not, in itself, indicate a reason to consider abortion.³

The policy of rubella immunization has been to eliminate primary infection in pregnant women and to prevent congenital infection. Since the first use of vaccine in 1969, there has been a drastic reduction in acquired rubella accompanied by an even greater reduction in the congenital form of the disease. The concept of herd immunity is proposed to reduce and eventually to eliminate the circulation of wild rubella virus. Theoretically, herd immunity means that the susceptible population is small enough so that an outbreak would not

From the Department of Family Practice and Community Health, University of Minnesota, Minneapolis, Minnesota. Requests for reprints should be addressed to Dr. Sharon Allen, Department of Family Practice and Community Health, 6-240 Phillips-Wangensteen Building, 516 Delaware Street SE, Box 381 Mayo, Minneapolis, MN 55455.

result if one person becomes infected or an imported case occurred. Even so, herd immunity would prevent major outbreaks, but not minor outbreaks in an actual population.⁴

The total eradication of congenital rubella syndrome has been the goal of the national immunization program. As evidenced, however, by the continuing cases of congenital rubella syndrome, this goal has not yet been met.

The US strategy currently is to vaccinate children prior to school entrance. The British strategy is to vaccinate only 11- to 14-year-old girls. Although more than 95 percent of children entering school have received rubella vaccine, the potential for rubella epidemics still exists among the postpubertal population. Outbreaks have occurred in hospitals, colleges, and universities. In fact, according to Orenstein et al in 1984,⁵ limited serological data suggest that susceptibility in the postpubertal population has not decreased substantially since the prevaccine era. Significant numbers of susceptible women remain at risk for rubella infection. In 1977, 70 percent of reported cases occurred in persons aged 15 years or older. Peak incidence rates are now moving from the 15- to 19-year-old to the 20- to 24-year-old group. Various authors show 9 to 24 percent of women of childbearing age to have nonprotective titers against rubella.^{4,6,7} The National Congenital Rubella Syndrome Registry estimates that currently more than 110 cases of congenital rubella syndrome occur annually. These cases are expected to incur a cost of more than \$24 million over their lifetime.⁵

Enforcing the current policy of preschool immunization will eventually ensure immunization levels adequate to eliminate rubella within the next 10 to 30 years. At present, however, significant numbers of susceptible childbearing women remain at risk for rubella infection and generation of infants with congenital rubella syndrome.

This study was designed to evaluate a sample population of childbearing women at risk for generation of infants with congenital rubella syndrome. Specifically, the purpose of the study was to (1) to identify the prevalence of rubella susceptibility in an educated, childbearing group of women at risk, (2) to determine the reliability of patient history in regard to immunization status, (3) to determine the patients' understanding of rubella, and (4) to review the present screening

policies and subsequent patient follow-up and compliance.

Methods

A total of 224 female students at the University of Minnesota Gynecological Health Clinic were asked to participate in the study. Informed consent was obtained from each subject. Subjects completed a study questionnaire to collect demographic information, medical information regarding their immune status, their history of pregnancy, miscarriage, and abortion, and their knowledge of rubella.

All participants had a rubella passive hemagglutination antibody test measured at the Minnesota State Health Department. Using department guidelines, an antibody titer of less than 1:8 was considered negative and therefore nonprotective against rubella infection. Participants whose tests were negative were sent a letter informing them about congenital rubella syndrome and offering free rubella immunization through the Gynecological Student Health Clinic. After six weeks charts were reviewed to determine follow-up immunization of seronegative participants. Data analysis was accomplished with the Statistical Package for the Social Sciences subprograms "crosstabs" and "frequencies." Statistical tests included chi-square and appropriate a posteriori analyses.

Results

Subject Demographics

The 224 university women students who participated ranged in age from 19 to 33 years (mean = 23.4). The results of blood serology as measured by rubella hemagglutination antibody titer showed 89 percent of the participants to be positive or immune and 10 percent to be negative or nonimmune and therefore at risk for rubella infection.

History of Infection or Immunization

Almost one half of the total participants were uncertain of their own history of rubella immunization or infection. Specifically, only 18 percent

Table 1. Patient History of Rubella Infection Compared With Serology Results

Patient History of Infection	Serology Results*	
	Positive No. (%)	Negative No. (%)
Yes	39 (97.5)	1 (2.5)
No	71 (91.0)	7 (9.0)
Unknown	88 (85.4)	15 (14.5)

* $\chi^2 = 4.46$, *df* 2, *P* > .05

Table 2. Patient History of Rubella Immunization Compared With Serology Results

Patient History of Infection	Serology Results*	
	Positive No. (%)	Negative No. (%)
Yes	43 (100.0)	0 (0)
No	38 (80.9)	9 (19.1)
Unknown	117 (89.3)	14 (10.7)

* $\chi^2 = 8.86$, *df* 2, *P* < .05

answered they had acquired rubella infection, 35 percent answered they had not, and 47 percent were uncertain. In response to the question concerning rubella immunization, 19 percent answered they had been immunized against rubella, 22 percent said they had not, and 59 percent were uncertain.

Analysis of data comparing patient history of infection or immunization status with serologic testing showed varying results. As depicted in Table 1, when results of serologic testing are compared with patient history of infection, the data results showed no association ($\chi^2 = 4.76$, *df* 2, *P* > .05). Patient history of infection appears to be unreliable in determining rubella immune status. However, data analysis comparing patient history of immunization with serology results showed a significant relationship ($\chi^2 = 8.86$, *df* 2, *P* < .05) as shown in Table 2. Although this result is statistically significant because of the large proportion (58.4 percent) of participants who were unsure of their immunization status, the interpretation of this significance is guarded.

Knowledge of the Disease

Next, the data were analyzed to determine participants' understanding of the disease termed *rubella* using a multiple-choice question. Sixty-eight percent of participants answered correctly, 3 percent chose incorrect answers, and 29 percent chose "unsure" as a response. As illustrated in Table 3 and Table 4, the association between patient history of infection and their knowledge of rubella, as well as association with their immuni-

zation status, is unclear because of the large percentage of unknowns.

When the results of serologic testing (the "gold standard" of immunity) were examined for a relationship to a right or wrong answer on the test question, there was no significant association ($\chi^2 = .137$, *df* 2, *P* > .05) (Table 3). This lack of significance suggests that knowing what the disease is and having had it (or being immunized against it) are independent of one another. Only within the group that had rubella positive serologic testing was there a relationship between knowledge of the disease and the self-reported history of immunization ($\chi^2 = 10.647$, *df* 2, *P* < .05) (Table 4). However, again because of the high proportion of unknowns (59.1 percent), some caution should be exercised in the interpretation of strength of this association. History of infection was not analyzed in this section because of some lacking data that prohibited reliable analysis. Finally, of those whose results on serological testing were negative, none reported having been immunized, but 19.2 percent who had positive serologic testing reported no history of immunization. Thus, there is a substantial risk of false negatives when relying on patient history for this information. False positives appear to be infrequent.

Additional Associations

Further characteristics of this sample population included data on the number of pregnancies, miscarriages, and abortions. These data were compared with serology testing results and showed no significance. At least one pregnancy was reported by 22.1 percent of the participants; in

Table 3. Comparison of Patient History of Infection to Knowledge of Rubella*			
Knowledge of Rubella Question	Patient History of Infection		
	Yes No. (%)	No No. (%)	Unknown No. (%)
Correct	35 (15.8)	54 (24.3)	62 (27.9)
Incorrect	5 (2.3)	24 (10.8)	42 (18.9)
* $\chi^2 = .137, df 2, P > .05$ (N/S)			

Table 4. Comparison of Patient History of Immunization to Knowledge of Rubella Within the Serology-Positive Group*			
Knowledge of Rubella Question	Patient History of Immunization		
	Yes No. (%)	No No. (%)	Unknown No. (%)
Correct	36 (23.8)	37 (24.5)	78 (51.7)
Incorrect	7 (9.9)	11 (15.5)	53 (74.6)
* $\chi^2 = 10.647, df 2, P < .05$			

this group, 6 percent were seronegative with prenatal screening and were not immunized in the postpartum period. One participant remained seronegative after four pregnancies. In the present study of the 23 identified seronegative participants, only 5 (21 percent) returned for free immunization. These data point out inadequacies in the present prenatal rubella screening methods as well as in compliance and follow-up.

Discussion

In this sample population, the resultant serologic testing showed a 10 percent prevalence of women who were nonimmune and therefore at risk for generation of infants with congenital rubella syndrome. This study is consistent with the literature showing 10 to 15 percent prevalence of patients with antibody titers insufficient to prevent rubella infection.

As seen by the data analysis, patient history of rubella infection was not reliable in predicting rubella immune status. Rubella infection may be very mild or even asymptomatic. Many people are possibly unaware or do not remember the disease event. Yet data analysis showed a significant relationship between history of rubella immunization and results of serologic testing. While it appears that participants actively immunized could correctly recall this fact, the significance remains unclear. Nearly 60 percent of participants were uncertain about their immune status. Patient history, therefore, appears inadequate to identify reliably the population at risk.

This unreliability confirms the need for serological testing for accurate determination of immune status. In this study, serological testing was done by the health department using the standard hemagglutination method. More sensitive measures are now available, including the enzyme-linked immunosorbent assay, ELISA.⁸ ELISA has the capability of detecting recent or primary expo-

sure (IgM reinforce) and past or secondary exposure (IgG reinforce). Although costs vary widely, hemagglutination methods are about one half the cost of IgM, IgG ELISA testing.

Approximately one third of the sample population answered "unsure" for the definition of rubella. It is interesting that those participants whose tests were seropositive and who could define rubella were statistically more reliable on their history of immunization. Perhaps patient education is justified, and awareness of rubella and congenital rubella syndrome should be included in health education in schools and communities.

At present, prenatal policy is to screen for rubella immunity at the first prenatal visit. If the patient is shown to be immune, the pregnancy is safe from risk of congenital rubella syndrome, but if the patient is not immune, immunization is delayed until postpartum.

Three of the 23 participants identified in this study as nonimmune reported at least one previous pregnancy. One participant had been pregnant four times and still remained nonimmune. In another study, approximately one third of mothers who gave birth to babies with congenital rubella syndrome have had a previous child.⁵ Theoretically, postpartum vaccination might prevent one third of the cases. Rubella screening results on prenatal charts should be documented prior to discharge postpartum just as rigorously as infants are screened for hypothyroidism and phenylketonuria.

Patient compliance is an important issue in rubella immunization efforts. In this study, participants with seronegative tests (10 percent) were notified by a letter explaining the risks of rubella infection during pregnancy and offered free immunization through the Student Health Service. However, only five of the 23 participants with seronegative test results returned for free immunization. The study was concluded in early summer, and participant noncompliance may have been partly due to students relocating. Also, some participants may have sought immunization elsewhere. A public health nurse with the Student Health Service continued to make contact with participants not responding to the study letter.

Several strategies have been proposed^{5,7} to immunize young women of childbearing age who are still at risk. To further reach susceptible individuals, screening and vaccination could be made

routine for primary care providers as well as at family planning clinics. Whenever possible, rubella immunity should be required. Susceptible hospital and clinic employees, both male and female (who may come in contact with pregnant patients), should be identified. Medical, physical therapy, and nursing students perhaps should have required rubella immunity for protection of both themselves and their patients.

Proof of rubella immunity should perhaps be a prerequisite for college admission. Men should also be included, since they can transmit disease to susceptible women. Military services require rubella immunity of recruits and have essentially eliminated rubella outbreaks common prior to this requirement.⁹

Since 1971 Colorado has required a premarital serologic test for rubella of all women applicants younger than 55 years old. The cost of this hemagglutination inhibition test is about \$1, and seronegativity rate is about 14.4 percent.¹⁰

Finally, a cost-effective plan would include immunization of populations at risk for congenital rubella syndrome and education of susceptible persons for the prevention of rubella and the consequences of congenital rubella syndrome.

References

1. Preblud SR, Serfula MK, Frank JA Jr, et al: Rubella vaccination in the United States: A ten-year review. *Epidemiol Rev* 1980; 2:171-194
2. Cooper LZ: Congenital rubella in the United States. In Krugman S, Gershon A (eds): *Symposium on Infections of the Fetus and Newborn Infant*. New York, Alan R. Liss, 1975, pp 1-22
3. Centers for Disease Control: Rubella vaccine: Recommendation of the Public Health Service advisory committee on immunization practices. *Ann Intern Med* 1978; 88:543
4. Hethcote HW: Measles and rubella in the United States. *Am J Epidemiol* 1983; 117:2-13
5. Orenstein WA, Bart KJ, Hinman AR, et al: The opportunity and obligation to eliminate rubella from the United States. *JAMA* 1984; 251:1988-1994
6. Robinson RG, Dadenhoeffer FE, Holroyd HS, et al: Rubella immunity in older children, teenagers, and young adults: A comparison of immunity in those previously immunized with those immunized. *J Pediatr* 1982; 101:188-191
7. Miller KA, Zager TD: Rubella susceptibility in an adolescent female population. *Mayo Clin Proc* 1984; 59:31-34
8. Fitzpatrick SB, Anthony R, Heald F: Serological response to rubella revaccination in adolescent females. *J Adolesc Health Care* 1983; 4:168-170
9. Crawford GE, Gremillion DH: Epidemic measles and rubella in air force recruits: Impact of immunizations. *J Infect Dis* 1981; 144:403-410
10. Judson FN, Shaw BS, Vernon TM Jr: Mandatory premarital rubella serologic testing in Colorado: A preliminary report. *JAMA* 1974; 229:1200-1202