Rubella Seroprevalence in Korean Children

The aim of this study was to determe the age-specific rubella seroprevalence and the related factors in Korean children. Subjects of the study were 5,393 students from 8 elementary schools in Gyeonggi Province, Korea. Questionnaire surveys with blood sampling were conducted in 1993, 1996, and 1999. ELISA tests, used to detect rubella specific IgG antibody, were Imx® (Abbott, U.S.A.) in 1993 and 1999, and Enzygnost® (Behring, Germany) in 1996. The age-adjusted rubella susceptibility rate was 22.9% (95% CI: 22.8-23.0%) and it increased with age from 14% to 28%. The susceptibility rates of vaccinees, nonvaccinees, and the unknown group were 21%, 35%, and 27%, respectively (p=0.000). The rates by parental education levels for elementary and below, middle school, high school, and college and over were 37%, 26%, 24%, and 20%, respectively. The geometric mean titers (GMTs) of nonvaccinees, the unknown group, and vaccinees were 47 IU/mL, 42 IU/mL, and 37 IU/mL, respectively (p=0.000). The susceptibility level was too high to prevent the rubella epidemic in Korea, which necessitates a programme that will enhance the coverage for 1st and 2nd MMR vaccination among school children. In particular, more attention should be paid to the vaccination of the children whose parental education level is relatively low.

Key Words : *Rubella; Seroepidemiologic Studies; Child; Social Class*

Moran Ki, Bo Youl Choi*,
Myoung-Hee Kim, Young-Jeon Shin*,
Taesung Park†

Department of Preventive Medicine, Eulji University School of Medicine, Daejon; *Department of Preventive Medicine, Hanyang University College of Medicine, Seoul; †Department of Statistics, Seoul National University, Seoul, Korea

Address for correspondence
Bo Youl Choi, M.D.
Department of Preventive Medicine, Hanyang University College of Medicine, 17 Haengdang-dong, Sungdong-gu, Seoul 133-791, Korea
Tel : +82.2-2290-0662, Fax : +82.2-2293-0660
E-mail : bychoi@hanyang.ac.kr

INTRODUCTION

The primary objective of a rubella immunization programme is to prevent the congenital rubella syndrome (CRS) (1). Vaccination programmes have eliminated or greatly decreased the rubella incidence and CRS in some developed countries (2-4). For example, since the licensure of the rubella vaccine in 1969, the numbers of reported cases of rubella and CRS have decreased by over 99% in the United States (2, 3).

However, by 1997, 78 countries (92% of industrialized countries, 36% of countries in economic transition, and 28% of developing countries) had included the rubella vaccine in their national immunization programmes (5). In Korea, rubella vaccine had not been incorporated into the national immunization programmes until 2000. However, measles, mumps, and rubella (MMR) vaccine has been distributed free of charge in public health centers for over 10 yr and used at private sectors with a charge. Since 1997, a two-dose MMR vaccination programme was recommended in Korea. The immunization rate of MMR has been over 80% since 1990 in a population under 2 yr, but the 2nd dose immunization rate was not high (<30%) among elementary school students (6).

Because rubella had not been a notifiable disease in Korea until 2000, there are insufficient data on the incidence of rubella and CRS. Like measles and mumps, rubella has also showed a periodic epidemic feature every 4-5 yr. During the outbreak from March to April 1996, 4,581 cases of rubella were reported to the national centers by temporary surveillance system (7). This outbreak also occurred among the vaccinated student population. To prevent CRS, knowledge on the rubella immunity in childbearing age women is important. However, it is not sufficient without information on the seroprevalence of children, because virus circulation usually begins among children to spread out to adults. Moreover, in spite of the immunization program for women at childbearing age, when virus circulation continues among children, a few susceptible pregnant women can be infected (8). Therefore, it is necessary to identify seroprevalence of children as a source of infection. The aim of the present study was to determine the age-specific rubella seroprevalence and the related factors among elementary school students from 1993 to 1999 in Gyeonggi Province, Korea.

MATERIALS AND METHODS

Study Subjects

The study area was Gyeonggi Province, which is 10 to 50 kilometers off Seoul, the capital city of Korea. We selected 8 elementary schools according to area, by recommendation of the Department of Education of the provincial office, all

of which included six grades to ensure the representativeness of Gyeonggi Province. Four of them are located in rural areas and the others in urban, and each of them represents eastern, western, southern, and northern areas of Seoul (Fig. 1).

We surveyed the students of these schools repeatedly in 1993, 1996, and 1999, incorporating questionnaires with serology tests. After testing rubella specific IgG antibody, we mailed the results to the nursing teachers of the schools and the parents of all study subjects. For students whose IgG antibody titer was very low, or negative, we administered the rubella vaccine free of charge with consent of their parents and then confirmed the serology of rubella after 5 weeks to 3 months. Thereafter we gave a second vaccination to the students who still remained negative for IgG antibody. The response rate for the questionnaire survey was 99.7% and that for the serological survey was 99.3%.

Questionnaires

We surveyed the general characteristics and the vaccination history, using questionnaires. Since the study subjects were elementary school students, their parents completed the questionnaires. We also reviewed the school health records and the personal vaccination records of the study subjects. However, most of the school records did not include data on MMR, because the vaccine was administered before school entry. Among the study subjects, the rate of available personal vaccination records were 30% in 1996 and 42% in 1999, and no information was available in 1993 when we did not review the records.

Serologic tests

After obtaining informed consents, blood samples were obtained through venipuncture. The sera were separated and stored at -70℃ until tested. Rubella-specific IgG antibod-

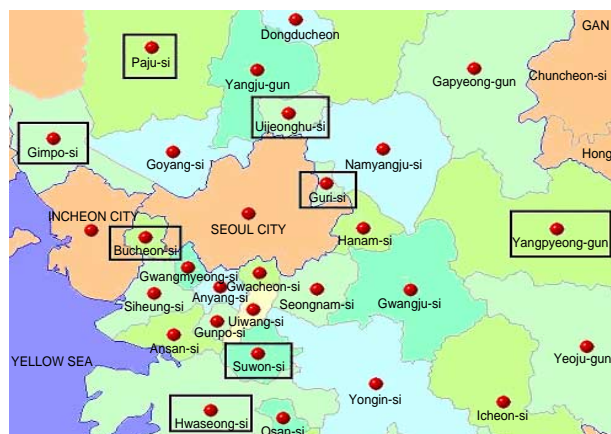
Fig. 1. Geographical distribution of schools involved in this study. Urban: Guri-si, Bucheon-si, Suwon-si, Uijeongbu-si; Rural: Yangpyeong-gun, Gimpo-si, Hwaseong-si, Paju-si.

ies were screened quantitatively with the use of commercial immunoassay kits (Imx® Abbott, U.S.A. in 1993 and 1999, and Enzygnost® Behring, Germany in 1996). Although they were not based on Korean population, the sensitivity, specificity, and accuracy of Abbott's Imx® were 99.9%, 98.9%, and 99.8%, respectively (9). For the Behring's Enzygnost®, the sensitivity and specificity were 100% and 98.5%, respectively (10). Even though all titers were calculated as IU/mL, there were possibilities of systematic error. Therefore, the comparison of titers was made by the year of survey.

Rubella specific IgG positivity indicates immunity against rubella. However, there are various opinions on the cut-off level for a definite immune status. In this study, we determined the positive level at 10 IU/mL and over, based on the Rubella Subcommittee of the National Committee for Clinical Laboratory Standards (NCCLS) (11).

Statistical Analysis

The data were analysed by using the Statistical Package SPSS® 10.0 for Windows. We used a 5% significance level. Seronegative samples were excluded in computing geometric mean titers (GMTs). We used the analysis of variance (ANOVA) model for the comparison of the GMTs. For comparison of the seronegativity between survey years, we calculated age-adjusted rates by direct method, using the Gyeonggi population in 1999. We used the chi-square test for comparing seroprevalence rates. We fit the logistic regression model for estimating age-adjusted odds ratios (OR).

RESULTS

General Characteristics of Study Subjects

Questionnaires and serological surveys were carried out in 8 elementary schools in 1993 (2,072 students), 1996 (1,665),

Table 1. Characteristics of children by survey year

Characteristics	Survey year (No., %)			
	1993 (n=2,072)	1996 (n=1,665)	1999 (n=1,656)	Total (n=5,393)
Gender				
Male	1,013 (49)	862 (52)	850 (51)	2,725 (51)
Female	1,059 (51)	803 (48)	806 (49)	2,668 (49)
Area				
Urban	1,097 (53)	1,030 (62)	939 (57)	3,066 (57)
Rural	975 (47)	635 (38)	717 (43)	2,327 (43)
Parental Education				
≤Primary school	131 (6)	26 (2)	19 (1)	176 (3)
Middle school	379 (18)	154 (9)	114 (7)	647 (12)
High school	997 (48)	818 (49)	928 (56)	2,743 (51)
≥College	333 (16)	382 (23)	430 (26)	1,145 (21)
Missing	232 (11)	285 (17)	165 (10)	682 (13)

Table 2. Rubella immunity status by survey year, age, and MMR vaccination

	1993		1996		1999		Total	
	No. (% total)	No. (%) seronegative	No. (% total)	No. (%) seronegative	No. (% total)	No. (%) seronegative	No. (% total)	No. (%) seronegative
Total	2,072 (100)	485 (22.4*)	1,070 (100)	423 (24.6*)	1,694 (100)	389 (21.5*)	5,393 (100)	1,297 (22.9*)
Age (yr)								
6	137 (7)	19 (14)	64 (4)	11 (17)	27 (2)	2 (7)	228 (4)	32 (14)
7	339 (16)	89 (26)	313 (19)	67 (22)	348 (21)	41 (12)	985 (18)	197 (20)
8	352 (17)	96 (27)	345 (21)	80 (23)	296 (17)	54 (19)	986 (18)	230 (23)
9	314 (15)	71 (23)	288 (17)	74 (26)	333 (20)	87 (26)	931 (17)	232 (25)
10	374 (18)	98 (26)	229 (14)	66 (29)	250 (15)	66 (27)	844 (16)	230 (27)
11	313 (15)	58 (19)	238 (14)	66 (28)	227 (13)	69 (31)	774 (14)	193 (25)
12	243 (12)	54 (22)	193 (12)	59 (31)	213 (13)	70 (33)	645 (12)	183 (28)
$p^†$		0.013		0.012		0.000		0.000
MMR Vaccination status								
Unvaccinated	395 (19)	134 (34)	98 (6)	42 (43)	93 (6)	32 (34)	586 (11)	208 (35)
Unknown	567 (27)	149 (26)	381 (23)	105 (28)	266 (16)	71 (27)	1,214 (23)	325 (27)
Vaccinated	1,110 (54)	202 (18)	1,186 (71)	276 (23)	1,297 (78)	286 (22)	3,593 (67)	764 (21)
$p^†$		0.000		0.000		0.000		0.000

*Age-adjusted rates by direct method using Gyeonggi Province population at 1999. $^†p$-value for the chi-square test.

Table 3. Crude and age-adjusted odds ratios (OR) for the association between related factors and the seronegativity for rubella

	No. (%) Seronegative	Crude OR	ORa*	95%CI	ORa†	95%CI
MMR Vaccination status						
Unvaccinated	208 (35)	2.0	2.0	1.6-2.4	–	–
Unknown	325 (27)	1.3	1.3	1.1-1.6	–	–
Vaccinated	764 (21)	1.0	1.0			
Survey year						
1999	389 (24)	1.0	1.0	0.86-1.2	1.3	1.0-1.5
1996	423 (25)	1.1	1.1	0.97-1.3	1.4	1.1-1.7
1993	485 (23)	1.0	1.0		1.0	
Gender						
Male	701 (26)	1.2	1.2	1.1-1.4	1.3	1.1-1.5
Female	596 (22)	1.0	1.0		1.0	
Area						
Urban	751 (25)	1.1	1.0	0.90-1.2	1.1	0.92-1.3
Rural	546 (24)	1.0	1.0	1.0		
Parental Education						
≤Primary School	65 (37)	2.3	2.2	1.5-3.0	2.3	1.4-3.7
Middle School	171 (26)	1.4	1.4	1.1-1.7	1.4	1.0-1.8
High School	646 (24)	1.2	1.2	1.0-1.4	1.1	0.90-1.3
Missing	185 (27)	1.5	1.4	1.2-1.8	1.3	0.90-2.0
≥College	230 (20)	1.0	1.0		1.0	

*Odds ratio adjusted only by age. †Odds ratio adjusted only by age among the vaccinees.

and 1999 (1,656). The gender distributions by survey year and age were not significantly different. The study subjects were 3,066 students (57%) for urban areas and 2,327 students (43%) for rural areas. Socioeconomic status was assessed by the education level of either the father or the mother, whichever was greater. Parental education levels had increased gradually over the survey years; the percentage as of middle school and below were 24% in 1993, 11% in 1996, and 8% in 1999

(Table 1). The range of age was 6 to 12 yr, and the distribution of age was not uniform. MMR vaccination rates by questionnaire were 54% in 1993, 71% in 1996, and 78% in 1999 (Table 2).

Rubella seroprevalence

The crude IgG antibody seronegative rate was 24.5% (1,297/5,393) and the 95% confidence interval (CI) by binomial distribution was from 22.9% to 25.2%. The overall rate standardized by direct method using the Gyeonggi Province population in 1999 was 22.9% (95% CI: 22.8-23.0%), and age-adjusted rates by the consecutive survey years were 22.4%, 24.6%, and 21.5% respectively. The differences between the survey years were not significant. However, seronegative rates by age were significantly different in 1993, 1996, and 1999, respectively, and the trends by age were significant in 1996 (p=0.002) and in 1999 (p=0.000); the older the subjects, the higher the negative rates. The seronegative rate of the vaccinees was 21%, and that of the nonvaccinees was 35%, while that of the unknown group ("do not know" or non-respondents group) was 27% (p=0.000) (Table 2).

The age-adjusted seronegative rates by vaccination status were also significantly different. The unvaccinated group had twice the risk of being seronegative and the unknown group had 1.3 times the risk compared with the vaccinated group. The crude and age-adjusted rubella seronegative rates over survey years were not significantly different. However, the age-adjusted seronegative rates among vaccinees in 1996 was 1.4 times higher than that of 1993.

Rubella-specific IgG negative rates by gender were 26% for male and 22% for female. The difference was still significant after age adjustment. Among vaccinees, age-adjusted
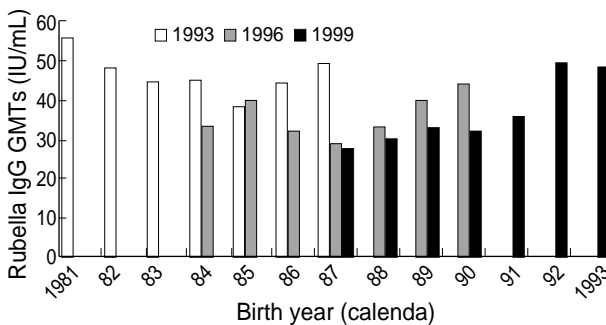
Fig. 2. Rubella IgG geometric mean titers (GMTs) of the seropositive population by survey year and birth year.
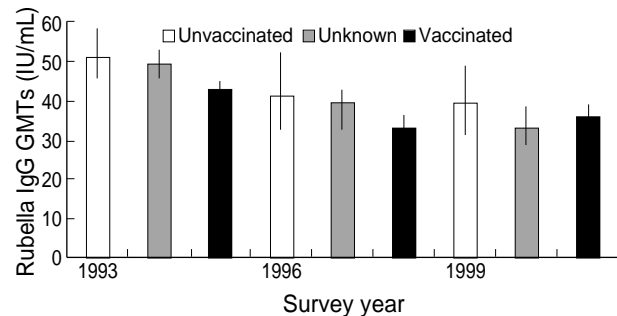

Fig. 3. Rubella IgG geometric mean titers (GMTs) and 95% confidence intervals of the seropositive population by the history of measles, mumps, and rubella (MMR) vaccination and survey year.

odds ratio of males against females was 1.3. Urban schools had more seronegative students than rural, but the difference was not significant. Rubella seronegative rates by parental education levels were 37% for elementary school and below, 26% for middle school, 24% for high school, 20% for college and over, and 26% for the missing group. The trend of high negative rates by parental education level, excluding the missing group, was statistically significant in 1993, 1999, and total. Age-adjusted odds ratio for parental education level of elementary school and below was 2.2 against the college and over group. The middle school graduated group had 1.4 times greater risk than the college and over group. The rate of the high school graduated group was not significantly different from that of the college and over group. Among vaccinees, the age-adjusted odds ratio for elementary school and below was 2.3, which was statistically significant (Table 3).

Rubella IgG antibody titer

The GMT in 1993 was 46 IU/mL, which was significantly higher than 34 IU/mL in 1996 and 36 IU/mL in 1999 ($p=$ 0.000). The GMTs by age were significantly different in all three survey years; "J" shaped distribution appeared in 1993 and 1996, and a significant linear association was shown in 1999. In 1999, the GMTs by birth year showed a decreasing pattern with increasing age (Fig. 2).

The GMTs by gender were not different. The GMTs of nonvaccinees were the highest followed by the unknown and vaccinees in 1993 ($p=0.001$) and 1996 ($p=0.002$). In 1999, the GMT of nonvaccinees was the highest also, but unknown group had the lowest titer ($p=0.274$). The GMTs of nonvaccinees, unknown group and vaccinees were 47 IU/mL, 42 IU/mL, and 37 IU/mL, respectively ($p=0.000$) (Fig. 3).

DISCUSSION

The study area, Gyeonggi Province reaches up to 10,135 km², which comprises 10% of the total area of Korea, and 9 million in population, which comprises 19% of Korean pop-

ulation in 1999. The gross product was 19.5% of the GNP (Gross National Product). The socioeconomic status of this area was estimated to be at the median of the whole Korea. Since the age distribution from 6 to 12 yr was not uniform, we compared the rubella immunity by the age-adjusted odds ratio. About 57% of the subjects lived in urban areas, which was significantly higher than 43% of those in rural areas. However, the vaccination coverage rate and rubella seroprevalence were similar between the urban and the rural because most cities of Gyeonggi Province are small and relatively new, so that the socioeconomic status of the urban areas was not much higher than that of the rural.

Seroprevalence rate was determined by the vaccination rate and the natural infection rate. A previous study conducted during 1986-88 for 5 to 14 yr old Korean adolescents reported susceptibility rates of 21.2% (n=824, ELISA of Abbott®) (12). In Korea, the rubella vaccine had been used popularly since 1985. Therefore, it is surprising that a similar high susceptibility rate was found; 22.9% in this study, compared to 21.2% in the previous report years prior to the popular use of the vaccine. Furthermore, after the rubella epidemic in 1996, the susceptibility rate of 1999 was still high enough for another epidemic occurrence. To prevent an epidemic of rubella, the herd immunity needs to be 83-85% at minimum. However, as the circulating virus decreased in highly vaccinated countries, the need for a much higher immunity level surfaced (13). So this susceptibility level evinces a sufficient condition for the rubella and congenital rubella syndrome epidemics to occur.

Many factors potentially influence the rubella susceptibility in child population. In the present analysis, rubella vaccination history, age, gender, and parental education level appeared to be significant factors in the acquisition of rubella antibody; residential area (urban or rural) did not appear to be significant. However, these findings need to be compared with those in other studies.

As expected, students with a rubella vaccination history had lower susceptibility rates than those with null or unknown history. The 21% susceptibility rate of those with a vaccination history is supposed to implicate a combination of an inaccu-

rate vaccination history and vaccine failure; it is impossible to separate the two in this analysis. Previous rubella vaccine studies have shown primary and secondary vaccine failure rates ranging from 0-11% and 1-22%, respectively (14-19). In Korea, primary vaccine failure rates also ranged from 0-12% (20-22). Among seropositive children, the GMT in the unvaccinated was the highest in all three survey years. The differences were statistically significant except in 1999. The GMT of the unvaccinated was from natural infection, so the highest titer in this group seems proper. The unknown group had a mixed effect of natural infection and vaccination, so the titer was lower than that in the unvaccinated group but higher than that in the vaccinated group. These results support the fact that the reinfection rate of the vaccinated group was higher than that of the naturally immune group (23). In 1996 and 1999, the susceptibility rate increased with age, which reflects the influence of vaccine. The younger age group had higher vaccination rates than the older age group. Among the vaccinees, the younger age group had the lower secondary vaccine failure. The GMTs could also be explained by vaccination effect. In 1999, since most of the seropositive students had immunity from vaccination, GMTs decreased with increasing age. In 1993, however, there was no linear association between age and susceptibility rate. This can be explained by the complex effect of vaccination and natural infection. The lower susceptibility in the younger age group might reflect the influence of vaccination, while the lower susceptibility of the older age group might reflect exposure to natural disease. The GMTs in 1996 and 1993 showed a "J" shape, which may be explained by the vaccination effect and the natural infection exposure effect. Students who had participated in the surveys (although they were not the same students), the GMTs of the previous survey were higher than those of the latter survey; which means that the titer decreased as time passed. This could explain the phenomenon that susceptibility increases with age in each survey as well as in the consecutive survey among the birth cohort.

Susceptibility rates were different by gender, which can be attributed to the immunologic effect. In our study, rubella immune loss rate during 3 yr was observed more frequently among boys (24). In the rubella epidemic of Korea in 1996, among 5 to 14 yr old, the incidence rate of boys (55/100,000) was higher than that of girls (19/100,000). In measles studies, the severity of disease and titers after vaccination were higher in females (25, 26). However, there was no relevant reference on rubella, so the gender factor is worth considering.

In this study, the susceptibility rates decreased with the increasing level of parental education. It can be explained by the fact that the children with parents of higher education had a higher vaccination rate. However, among the vaccinees, the susceptibility rate of those whose parental education level was elementary school and below was higher. This might be explained by inaccurate vaccination histories of the elementary school and below group. Another explanation is a higher vac-

cine failure in the lower socioeconomic group, the lower socioeconomic group might not have received timely vaccination, and had less booster vaccinations (27). The group that had been vaccinated too early or too late caused more primary vaccine failures, and the group that had less booster vaccination had more secondary vaccine failures. A large Mexican seroepidemiological study showed a significant increase in susceptibility as the educational level decreased (28). However, among the unvaccinated population of Turkey, urban residence area and higher socioeconomic groups were reported to have lower susceptibility, but the socioeconomic factor was not statistically significant (29). Therefore, the effect of socioeconomic status is different by country. This can be explained by the difference of living conditions and adequate vaccination rates according to the socioeconomic status.

In conclusion, we observed a high susceptibility for rubella in all three surveys, as well as in the period prior to the vaccine programme. It was explained by the insufficient vaccination coverage rate and vaccine failure. Especially, 21% susceptibility rate in the vaccinated group necessitates a booster rubella vaccination. At the same time, the lower socioeconomic group had a significantly higher susceptibility rate in spite of vaccination. In the coming years, serosurveillance studies should focus on high-risk population, such as the lower socioeconomic group. To reach an enough level of herd immunity, more effort is needed to increase the vaccination coverage rate.

REFERENCES

1. Center for Disease Control and Prevention. *Measles, mumps, and rubella-vaccine use and strategies for elimination of measles, rubella, and congenital rubella syndrome and control of mumps: Recommendation of the Advisory Committee on Immunization Practices (ACIP). MMWR 1998; 47: 1-57.*

2. Center for Disease Control and Prevention. *Rubella and congenital ruella syndrome: United States, Jan 1,1991-May 7, 1994. MMWR 1994; 43: 397-401.*

3. Center for Disease Control and Prevention. *Rubella and congenital rubella syndrome: United States, 1994-1997. MMWR 1997; 46: 350-4.*

4. Peltola H, Heinonen OP, Valle M, Paunio M, Virtanen M, Karanko V, Cantell K. *The elimination of indigenous measles, mumps, and rubella from Finland by a 12-year, two-dose vaccination program. N Engl J Med 1994; 331: 1397-402.*

5. Robertson SE, Cutts FT, Samuel R, Dias-Ortega JL. *Control of rubella and congenital rubella syndrome (CRS) in developing countries. Part 2: vaccination against rubella. B World Health Org 1997; 75: 69-80.*

6. Ministry of Health and Welfare. *Expanded Program on Immunization (EPI). The annual report of health and welfare, 2000. Available from URL: http://www.mohw.go.kr/hp/owa*

7. National Institute of Health-Korea. *Communicable Diseases Monthly Report. Seoul: National Institute of Health-Korea, 7, 1996.*

8. Pecham C. *Congenital rubella in the United Kingdom before 1970:*

the preventive era. *Rev Infect Dis 1985; 7: S11-6.*

9. Schaefer LE, Dyke JW, Meglio FD, Murray PR, Crafts W, Niles AC. *Evaluation of microparticle enzyme immunoassays for immunoglobulins G and M to rubella virus and Toxoplasma gondii on the Abbott Imx automated analyzer. J Clin Microbiol 1989; 27: 2410-3.*

10. Behring. *Enzygnost Anti-Rubella-Virus/IgG Package Insert, 1998.*

11. Skendzel LP. *Rubella Immunity. Defining the level of protective antibody. Am J Clin Pathol 1996; 106: 170-4.*

12. Lee IS, Kim CH, Lee SJ, Cho TH. *Measurement of serum rubella antibody titers in Korean children, female adolescents, and pregnant women. Asia Oceania J Obstet Gynaecol 1992; 18: 345-53.*

13. Fine PEM. *Herd Immunity: History, Theory, Practice. Epidemiol Rev 1993; 15: 265-302.*

14. Balfour HH Jr, Groth KE, Edelman CK. *RA27/3 Rubella vaccine, a four year follow-up. Am J Dis Child 1980; 134: 350-3.*

15. Asahi T, Ueda K, Hidaka Y, Miyazaki C, Tanaka Y, Nishima S. *Twenty-three year follow-up study of rubella antibodies after immunization in a closed population, and serological response to revaccination. Vaccine 1997; 15: 1791-5.*

16. Chu SY, Bernier RH, Stewart JA, Herrmann KL, Greenspan JR, Henderson AK, Liang AP. *Rubella antibody persistence after immunization: sixteen-year follow-up in the Hawaiian Islands. JAMA 1988; 259: 3133-6.*

17. O'Shea S, Best JM, Banatvala JE, Marshall WC, Dudgeon JA. *Rubella vaccination: persistence of antibody for up to 16 years. Br Med J 1982; 285: 253-5.*

18. Christenson B, Bottiger M. *Long-term follow-up study of rubella antibodies in naturally immune and vaccinated young adults. Vaccine 1994; 12: 41-5.*

19. Knox EG. *Theoretical aspects of rubella vaccination strategies. Rev Infect Dis 1985 (Suppl 1); 7: S194-7.*

20. Choi B, Shin YJ, Park HB, Yoon BJ, Hahn JS. *A study on the positive rate of rubella antibody and the sero-conversion rate after rubella vaccination: students of 9 girls' high schools in Gyeonggi-do, Korea. Korean J Epidemiol 1993; 14: 173-84.*

21. Park KS, Kim HS. *Seroprevalence of rubella antibodies and effects of vaccination among healthy university women students in Korea. Yonsei Med J 1996; 37: 420-6.*

22. Min CH, Lee JH, Cho MK. *A study of immunogenicity of measles, mumps and rubella vaccine prepared from human diploid cell. J Korean Soc Microbiol 1991; 26: 487-91.*

23. Horstmann DM, Liebhaber H, Le Bouvier GL, Rosenberg DA, Halstead SB. *Rubella reinfection of vaccinated and naturally immune persons exposed in an epidemic. N Engl J Med 1970; 283: 771-8.*

24. Ki MR, Kim MH, Choi BY, Shin YJ, Park TS. *Rubella antibody loss rates in Korean children. Epidmiol Infection 2002; 129: 557-64.*

25. Black FL. *Measles. In: KR Evanse AS, ed. Viral infections of humans, epidemiology and control. 4 ed. New York: Plenum publishing Co, 1997.*

26. Brody JA, Sever JL, Edgar A, McNew J. *Measles antibody titer in multiple sclerosis patient and their siblings. Neurology 1972; 22: 492-9.*

27. Ki MR, Kim MH, Shin YJ, Choi BY. *MMR immunization rate and related factors. J Korean Pediatr Soc 2001; 44: 375-88.*

28. Gutierrez Trujillo G, Munoz O, Tapia Conyer R, Bustamante Calvillo ME, Alvarez y Munoz MT, Guiscafre Gallardo JP, Magos C, Sepulveda J. *The seroepidemiology of rubella in Mexican women; a national probability survey. Salud Pubilica Mex 1990; 32: 623-31.*

29. Aksit S, Egemen A, Ozacar T, Kurugol Z, Keskinoglu P, Tasbakan M, Caglayan S. *Rubella seroprevalence in an unvaccinated population in Izmir: recommendations for rubella vaccination in Turkey. Pediatr Infect Dis J 1999; 18: 577-80.*