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MEASLES ANTIBODY RESPONSE IN VACCINATED CHILDREN*

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SUMMARY: Evliyaoğlu N, Altıntaş D, Kılıç NB, Alhan SE, Önenli N, Güneşer S, Bahçebaşı T. (Social Pediatrics Unit, Department of Pediatrics, Çukurova University Faculty of Medicine, Adana, Turkey). Measles antibody response in vaccinated children. Turk J Pediatr 1996; 38: 315-321.

The incidence of measles has declined in our country since the routine administration of measles vaccination was initiated. However, measles outbreaks have been observed even among previously vaccinated children. The objective of this study was to evaluate the measles antibody response of children vaccinated at nine months of age. Measles-specific IgG antibodies were determined by enzyme-linked immunosorbent assay. Of 345 children tested, 20.3 percent were immunologically measles-susceptible. When measles-specific antibody titers were analyzed with respect to the elapsed time since prior vaccination, the result was found to be insignificant ($p>0.05$). These data suggest that the underestimated seropositivity rate of measles antibody may be related to both primary vaccine failure and inappropriate vaccination age. *Key words: enzyme-linked immunosorbent assay, measles antibodies, measles vaccine, vaccine failure.*

Although preventable, measles remains a disease with the potential to cause serious morbidity and mortality. It continues to be a significant public health problem in the world. WHO estimates that approximately 1.4 million children die of measles every year[1]. The measles vaccine prevented an estimated 52 million cases of measles during the first 20 years of its use and measles complications declined more than 99 percent from the prevaccine era[2].

By 1978, it was believed that measles could be eliminated from the United States in the near future[3]; however, continued measles outbreaks have induced public

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health authorities to review measles vaccination strategies. In Turkey, a single-dose vaccination at nine month of age is being administered, as recommended by WHO[1]. The incidence of measles has declined in our country since 1985 when measles immunization campaigns were initiated. Nevertheless, measles outbreaks have continued in recent years. In 1991, 22,521 measles cases were reported in our country[1]. In the 1990s, measles outbreaks have usually been observed among preschool and school-age children who were previously vaccinated. In Adana, vaccine coverage for children between the ages of one and nine years was recently found to be 80 percent as compared to 85% percent in 1992[4]. Thus, we planned this pilot study to determine the measles antibody response of children vaccinated at nine months of age.

Material and Methods

Study population

All children from four health departments who had been vaccinated at nine months of age with live measles vaccine were eligible for participation in this study. A total of 345 children (181 boys, 164 girls) between the ages of one and 10 were included in the study. Birth date, sex and date of measles vaccination were ascertained from each subject. Children were excluded from the study if they had 1) received more than one measles vaccine; 2) had had any disease known by their family as measles or compatible with it.

The study population was grouped according to the interval since measles vaccination (0-2; 3-4; 5-6; 7-8; 9-10 years). The number of children in each group was 65, 80, 69, 74 and 57, respectively.

Specimen collection

Serum samples were collected by venipuncture, centrifuged and stored at –20°C.

Antibody titers

Measles-specific IgG antibodies were detected by a direct binding enzyme-linked immunosorbent assay (ELISA), which is both sensitive and specific (100%) for the detection of measles-specific antibodies. Clin-ELISA (Incstar Corporation, Stillwater, Minnesota, USA) commercial test kits were used for the detection of anti-rubeola antibodies. Absorbances of the serum samples were read at 405 nm and converted to ELISA values using a test-fit linear regression program. If an ELISA value was equal to or greater than 110, it was considered to be positive. Alls samples for which ELISA values were between 101 and 108 were repeated. If an ELISA value was 100 or less, it was considered to be negative.

Statistical analysis

Comparisons were evaluated using chi-square and t test with corresponding p values. Hypothesis tests for population proportions were made by calculating the z-statistics. The significance level was defined as $p<0.05$.

Results

Subjects

Serum samples were obtained from 345 children, 181 (52.5%) male and 164 (47.5%) female. There were no significant differences with regard to sex ($p>0.05$).

IgG Titers

The distribution of ELISA test results is shown in Table I. Although the highest positivity rate for anti-rubeola IgG antibody was found in the fifth group, there was no statistically significant difference between the groups ($X^2=6.49$, $p>0.05$).

Table I: ELISA Test Results in the Study Groups

Study groups	Interval (years)	No. of samples			IgG results		Mean ELISA value of positive samples
		Male	Female	Total	No. of positive (%)	No. of negative (%)	
I	0-2	36	29	65	55 (84.6)	10 (15.4)	247
II	3-4	41	39	80	60 (75.0)	20 (25.0)	224
III	5-6	32	37	69	52 (75.4)	17 (24.6)	234
IV	7-8	38	36	74	59 (79.7)	15 (20.3)	229
V	9-10	34	23	57	49 (85.9)	8 (14.1)	242
Total	0-10	164	181	345	275 (79.7)	70 (20.3)	

ELISA values of the anti-rubeola IgG-antibody-positive samples in the study groups can be seen in Fig. 1. The highest ELISA value was 580, and it was found in a 16-month-old girl who had been vaccinated seven months previously. The mean ELISA values of the positive samples are shown in Table I. Group I included children vaccinated recently (within past 24 months) who had the highest mean ELISA values. No statistically significant difference was found between the groups.

Among 345 children, 55 (84.6%) of the 65, 60 (75.0%) of the 80, 52 (75.4%) of the 69, 59 (79.7%) of the 74 and 49 (86.0%) of the 57 in the study groups, respectively, were seropositive. While a total of 275 (79.7%) of the 345 children

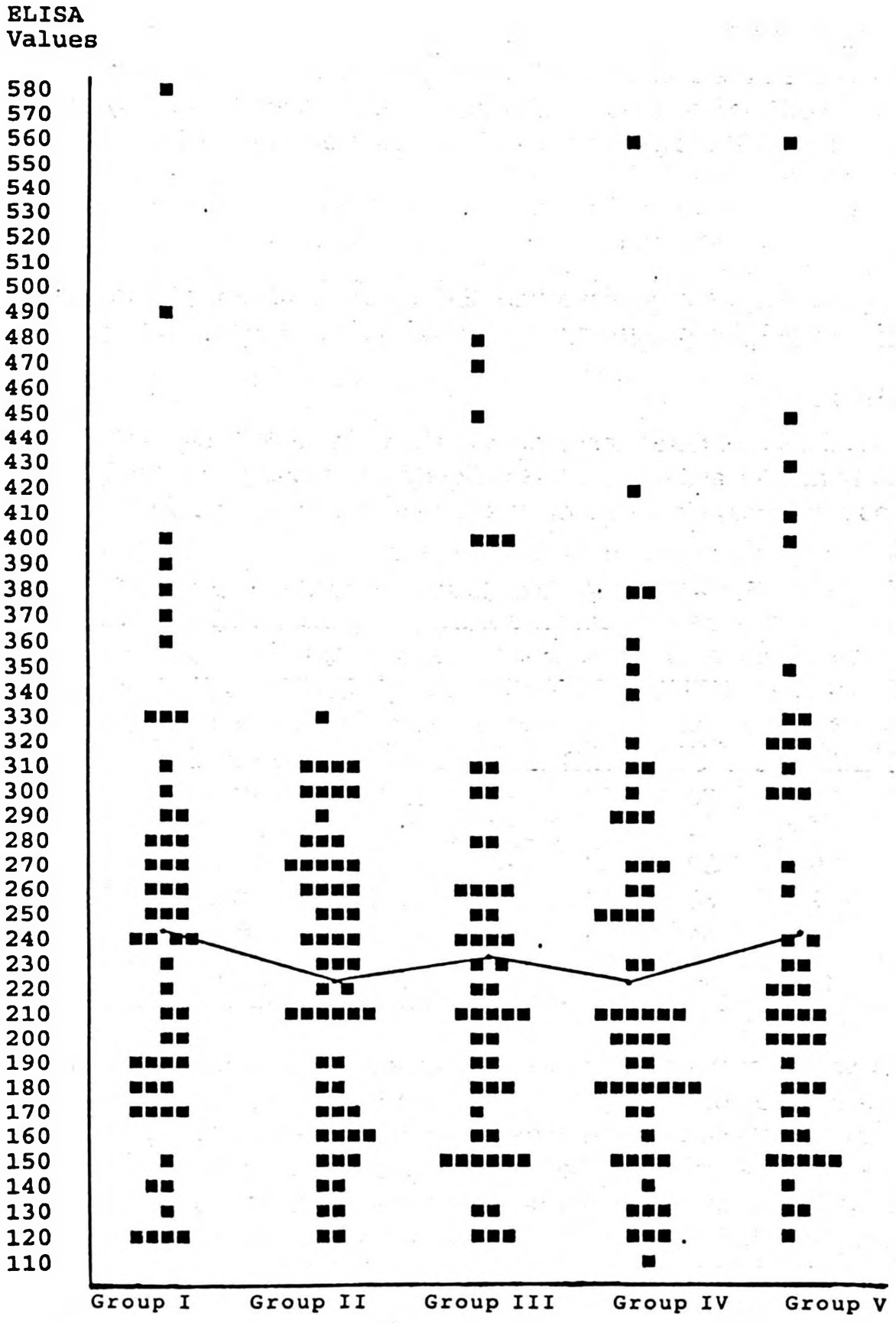

Fig. 1: ELISA values in positive samples.
(*): Mean ELISA values of the groups.

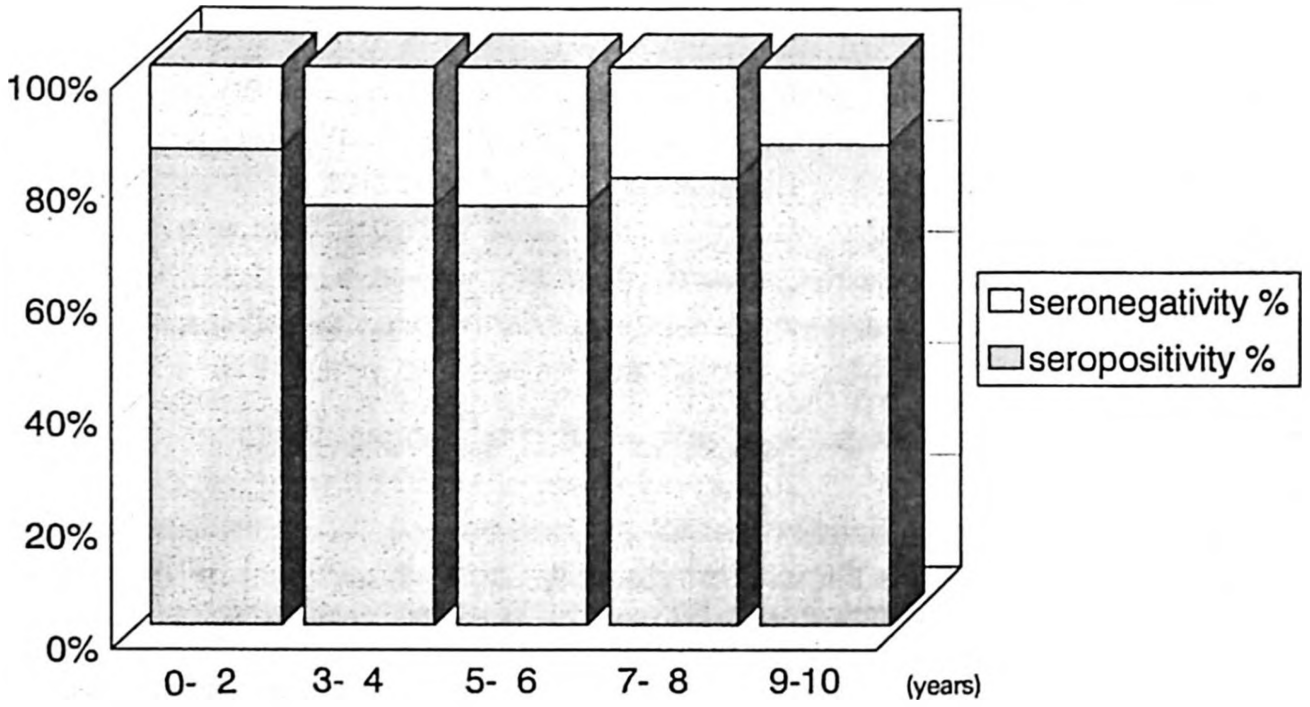

Fig. 2: Distribution of results.

were seropositive, 70 (20.3%) children who were known to have been vaccinated previously proved to have no detectable ELISA antibody. The ratios of serologic tests are shown in Fig. 2.

The vaccine seropositivity rate (78.7%) in our study when compared with a similar study in Adana in 1992 was found to be significant according to z test ($t=7.5$, $p<0.05$).

Discussion

Although a very effective measles vaccine is being used, measles has not yet been eliminated. The major problem of measles elimination is vaccine failure, which can be primary or secondary. Secondary vaccine failure occurs when immunity is lost after initial seroconversion. Though secondary vaccine failure has been reported most frequently in recipients of killed-measles vaccine, it may also occur in recipients of live measles vaccine[3,5]. Waning immunity may be responsible for the increased number of cases in school-age children[8].

In our study, by comparing the immunologically measles-susceptible subjects who were grouped according to two-year intervals since vaccination, we could not find statistically significant differences. We suggest that immunity to measles remained the same for nine years in our vaccinated children. Weibel et al.[7] concluded that the patterns of antibody persistence 7.5 years after administration of combined measles-mumps-rubella were the same and that there was no alteration in the retention of immunity. In Krugman's[8] prospective study of immunologic response of 47 children who had natural measles and 70 children immunized with live measles vaccine it was revealed that immunity persisted 16 years after immunization as well as after natural measles infection. In other investigations, vaccine failure was not associated with the time elapsed since vaccination[9,10]. On the contrary, several other studies have suggested that the duration of immunity derived from vaccination may not be as long-lasting as that from natural infection[11,12]. More studies are needed to prove this suggestion.

The principal cause for the measles epidemic in previously vaccinated persons is primary vaccine failure[13,14]. The known reasons for primary vaccine failure include residual transplacental maternal antibodies which inhibit vaccine virus replication and resulting sufficient antigenicity, and vaccine virus inactivation caused by inappropriate vaccine storage or handling.

Serological surveys have demonstrated rates of postvaccination seroconversion as high as 95 percent in several studies[3,15,18]. Orenstein et al.[17], seroprevalence was 98.6% percent for measles antibodies in high school students who had been immunized after 14 months of age with a single dose of measles.

We found 79.7 percent seroconversion in 345 children vaccinated at nine months of age. This result was statistically higher than that of the 1992 study in Adana[4]. Though our vaccine failure rate seems to be lower than that reported in 1992, it is actually a higher rate, since the estimated rate was only two to 10 percent[18]. We believe that the vaccination age may alter this result, because the inhibitory effect of maternal antibodies persists until nine to 12 months[18-21]. Vaccination before the age of 12 months may be a risk factor for vaccine failure.

The results of this study suggest the need for some new precautions and further studies:

1. In order to increase measles vaccine coverage and efficacy, all children at the recommended age should be vaccinated, and the persons and associations who administer the vaccination should be educated.

2. The exact elimination time of maternal antibodies in children must be determined so that the appropriate age for measles vaccination in Turkey can be established.

3. To prevent measles outbreaks in school-age children, revaccination policy should be reevaluated.

REFERENCES

1. World Health Organization. Expanded programme on immunization. Measles control a global battle in progress. Switzerland. Wkly Epidemiol Rec 1993; 23: 1-6.
2. Bloch AB, Orenstein WA, Statler HC, et al. Health impact of measles vaccination in the United States. Pediatrics 1985; 76: 524-532.
3. Birkhead GS, Morse DL, MillS IJ, Novick LF. New York State's two-dose schedule for measles immunization. Public Health Rep 1991; 106: 338-344.
4. Bahçebaşı T. Adana'da kızamık ve kontrolu. Adana Sağlık Dergisi 1993; 3: 5-20.
5. Frank JA Jr, Orenstein WA, Bart KJ, et al. Major impediments to measles elimination. The modern epidemiology of an ancient disease. Am J Dis Child 1985; 139: 881-888.
6. Gaur S, Kesarwala H, Gavai M, et al. Immunoprophylaxis: use of vaccines. Pediatr Clin North Am 1994; 41: 754-758.
7. Weibel RE, Buynak EB, McLean AA, et al. Persistance of antibody after administration of monovalent and combined live attenuated measles, mumps and rubella virus vaccines. Pediatrics 1978; 61: 5-11.
8. Krugman S. Further-attenuated measles vaccine: characteristics and use. Rev Infect Dis 1983; 5: 477-481.
9. Wittler RR, Veit BC, McIntyre S, Schydlower M. Measles revaccination response in a school-age population. Pediatrics 1991; 88: 1024-1030.
10. Hull HF, Montes JM, Hays PC, Lucero RL. Risk factors for measles vaccine failure among immunized students. Pediatrics 1985; 76: 516-523.
11. King JC Jr, Lichenstein R, Feigelman S, et al. Measles, mumps and rubella antibodies in vaccinated Baltimore children. Am J Dis Child 1993; 14': 556-560.
12. Centers for Disease Control. Measles prevention. Recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR 1989; 38: 1-18.
13. Peter G. Measles immunization: recommendations, challenges, and more information. JAMA 1991; 265: 2111-2112.
14. Markowitz LE, Preblud SR, Fine PE, Orenstein WA. Duration of live measles vaccine-induced immunity. Pediatr Infect Dis J 1990; 9: 101-110.
15. Lepow ML. Measles vaccine and measles control. Pediatric Ann 1990; 19: 543-545, 548-550.
16. Gustafson TL, Lievens AW, Brunell PA, et al. Measles outbreak in a fully immunized secondary-school population. N Engl J Med 1987; 316: 771-774.
17. Orenstein WA, Herrmann K, Albrecht P, et al. Immunity against measles and rubella in Massachusetts school-children. Dev Biol Stand 1986; 65: 75-83.
18. American Academy of Pediatrics, Committee on Infectious Diseases. Measles: reassessment of the current immunization policy. Pediatrics 1989; 84: 1110-1113.
19. Ceyhan M, Kanra G, Vargel S, Işıkçelik Y. The evaluation of vaccination against measles at nine months of age. Report of an epidemic. Turk J Pediatr 1992; 34: 127-133.
20. Orenstein WA, Markowitz L, Preblud SR, et al. Appropriate age for measles vaccination in the United States. Dev Biol Stand 1986; 65: 13-21.
21. Mast EE, Berg JL, Hanrahan LP, et al. Risk factors for measles in a previously vaccinated population and cost-effectiveness of revaccination strategies. JAMA 1990; 264: 2529-2533.