Measles Antibody in the Children in Ubon Ratchathani Province

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Abstract

Measles is a highly contagious disease, preventable by vaccine. Measles epidemics have been dramatically controlled since the introduction of live attenuated measles vaccine. Measles antibody is used as an indicator of previous natural infection or vaccination, and also as a marker of protective immunity. The authors determined measles IgG levels in 1,176 children in Ubon Ratchathani province by ELISA from September 1998 to January 1999. Two- hundred and sixty- five cases (22.5%) had antibodies below the protective level (< 320 mIU/ml). Antibodies were high during the neonatal period, then declined to below the protective level at 4-6 months of age, and were negative at age 7-11 months. An increase in antibody level after 1 year old might be the result of measles immunization at 9-12 months of age, then antibodies decreased to the lowest level at 3-5 years after immunization or 4-6 years of age. A second dose of immunization will increase the number of children who have antibodies above the protective level better than one dose of immunization and it is recommended to revaccinate at 4-6 years of age. There was no statistical difference of measles antibody between boys and girls in all age groups.

Key word : Measles Antibody, Children, Ubon Ratchathani Province

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Measles is a highly contagious disease caused by the rubeola virus. The disease usually occurs in children, and is characterized by cough, coryza and fever. Koplik's spot which precedes the onset of rash, is pathognomonic for measles. Recovery from the disease occurs within one week, but sometimes serious complications of respiratory and the central nervous system may occur. Natural measles virus infection induces lifelong immunity, and a second attack of measles is rare. Measles in the U.S.A. has been dramatically controlled since the introduction of the live attenuated measles vaccine in 1963, but a serious problem still remains in developing countries[1-3]. The measles virus initially induces IgM response followed by IgG[4,5]. Specific antibody to viral protein can be measured by immunoprecipitation, complement fixation (CF) test and enzyme linked immunosorbent assay. (ELISA). The most abundant and most rapidly produced antibody is that against the nucleocapsid [N] protein, and it is the major antibody detected in the CF test. Because of the abundance of anti-N antibody, its absence is the most accurate indicator for seronegativity. The presence of measles antibody is used as an indicator for previous natural infection or measles vaccination. It is also a suggestion of protective immunity. Humoral immunity is important in preventing measles infection, but cellular immune response appears to be important in aborting clinical symptoms during acute infection[6,7].

The authors conducted this study on the detection of the measles antibody in children in Ubon Ratchathani, a province in the northeast of Thailand with a population of 1.8 million, in order to determine the appropriate age- group for the second measles immunization dose.

MATERIAL AND METHOD

Study population

During the period between September 1998 to January 1999, a total of 1,176 children (637 boys and 539 girls) with an age-range of 1 day to 15 years were recruited from the Well Baby Clinic at Sappasittiprasong Hospital, which is a regional hospital in Ubon Ratchathani province, and also from health centers in 5 districts in the same province. The parents were counselled and interviewed for history of measles immunization of their children. Written consent form was needed for enrollment to the study.

Antibody testing

Half ml of blood was collected from each child; serum was separated and stored at 4-6°C until tested. Detection for measles IgG was performed at the National Institute of Health, Department of Medical Sciences, Ministry of Public Health by ELISA using Enzygnost® reagent (Date Behring, Germany).

Statistical analysis

Data were analyzed by EPI INFO version 6.0 using number, percentage, mean, standard deviation, χ^2 and student T test. Measles antibody titer of ≥320mIU/ml was defined as criteria for the protective level against measles virus infection[8,15,16].

RESULTS

It was found that 265 (22.5%) of 1,176 children studied had a measles antibody level below 320 mIU/ml, and the overall mean level was 3306.7 mIU/ml. There were 1,033 (87.8%) of 1,176 children who received measles or mumps-measles-rubella vaccination, and 896 (86.7%) of 1,033 children received 1 dose, 137 (13.3%) of 1,033 children received 2 doses.

Detection of measles antibody in children of different age-groups

Measles antibody level was high during the newborn period, and gradually decreased to unprotective level at age 4-6 months before disappearing at 7-11 months of age. After the child received the first dose of measles or mumps-measles-rubella vaccine, the measles antibody rose sharply and remained above protective level up to the age of 15 years. Means of measles antibody level by different age-groups is shown in Table 1.

Statistical difference in level of the measles antibody between boys and girls was not observed in all age-groups (p- value > 0.05) as shown in Table 2.

Measles antibody in non-vaccinated and vaccinated children

It was found that 66 (46.1%) of 143 children in the non-vaccinated group had antibodies above the protective level. There were 725 (81.1%) of 896 children who had antibodies above the protective level after they received one dose of measles

Table 1. Detection for measles antibody in children of different age – groups.

Age-groups	Number of study cases	Number of cases with measles antibody ≥ 320 mIU/ml	%	* Measles antibody level (mIU/ml) Mean ± SD
1 day – 1 month	31	31	100	6145.16 ± 580.39
2 – 3 months	35	25	71	1344.86 ± 286.80
4 – 6 months	55	9	16	129.83 ± 29.84
7 – 11 months	23	0	0	0.00
1 – 3 years	178	149	83.7	2268.31 ± 224.49
4 – 6 years	256	197	76.9	3130.86 ± 258.04
7 – 9 years	227	199	87.6	3055.37 ± 253.88
10 – 12 years	229	170	87.6	4425.37 ± 429.76
13 – 15 years	142	121	85.2	5118.03 ± 366.35

* Determined from average antibody in all cases in different age – groups.

Table 2. Levels of measles antibody by sexes.

Age – group	Number of study cases (Boys)	Number of cases with measles antibody ≥ 320 mIU/ml% (Boys)	%	* Measles antibody level Boys (Mean ± SD)	Number of study cases (Girls)	Number of cases with measles antibody ≥ 320 mIU/ml% (Girls)	%	* Measles antibody level Girls (Mean ± SD)	P - Value
1 day – 1 month	15	15	100	6,666.67 ± 869.68	16	16	100	5,656.25 ± 781.40	0.38
2 – 3 months	22	15	68.18	1,409.09 ± 348.09	13	10	76.9	1,236.15 ± 516.76	0.77
4 – 6 months	27	7	25.9	180.37 ± 43.94	2	2	0.7	81.07 ± 39.05	0.08
7 – 11 months	15	0	0	0.00 ± 0.00	8	0	0.0	0.0 ± 0.00	0.00
1 – 3 years	96	59	61.4	2,314.38 ± 288.44	82	68	82.9	2,214.39 ± 353.20	0.82
4 – 6 years	152	115	75.6	3,096.58 ± 349.71	104	82	78.8	3,180.96 ± 379.09	0.86
7 – 9 years	122	105	86.0	3,243.93 ± 362.24	105	94	89.5	2,836.29 ± 352.94	0.42
10 – 12 years	136	105	77.2	4,196.18 ± 608.20	93	75	80.6	4,760.54 ± 575.56	0.52
13 – 15 years	52	49	94.2	5,612.12 ± 601.94	90	72	80.0	4,832.56 ± 461.53	0.30

* Determined from average antibody in all cases in different age – groups.
There was no statistical difference of measles antibody between boys and girls in all age-groups at p = 0.05

or mumps-measles-rubella vaccine and 120 (87.1%) of 137 children had antibodies above the protective level after they received two doses of vaccine. Statistical difference in level of measles antibodies between subjects who received one or two doses of vaccine was not observed (p-value> 0.05) as shown in Table 3.

Levels of measles antibody at different times after one dose vaccination

After the child received the measles or mumps-measles-rubella vaccine, measles antibodies rose sharply, then at 37-60 months or 3-5 years after vaccination, measles antibodies decreased to the lowest level. There was a decreased number of children who had antibodies above the protective level to the lowest level in this group as shown in Table 4.

DISCUSSION

In Thailand, a measles epidemic was first observed in 1984 with an incidence rate of 93.67/ 100,000 population. In that year, the Ministry of Public Health introduced the measles vaccine into the Expanded Programme on Immunization [EPI]. Since then, the incidence of measles has declined

Table 3. Measles antibody in non-vaccinated and vaccinated children.

History of measles vaccination	Number of cases with measles antibody level < 320 mIU/ml	%	Number of cases with measles antibody level ≥ 320 mIU/ml	%	Total cases
No vaccination (Newborn – 11 Months)	77	53.9	66	46.1	143
Measles or Mumps-Measles-Rubella 1 dose	171	18.9	725	81.1	896
Measles or Mumps-Measles-Rubella 2 doses	17	12.9	120	87.1	137
Total	265	22.5	911	77.5	1,176

$\chi^2 = 3.558$ p = 0.1183

Table 4. Levels of measles antibody at different times after one dose vaccination.

Time after measles vaccination	Number of study cases	Number of cases with measles antibody ≥ 320 mIU/ml	%
0 – 12 months (0 – 1 year)	110	92	83.64
13 – 36 months (1 – 3 year)	81	66	81.48
37 – 60 months (3 – 5 years)	196	146	74.48
61 – 84 months (5 – 7 years)	85	72	84.71
85 – 108 months (7 – 9 years)	75	60	80
109 – 132 months (9 – 11 years)	162	133	82.09
133 – 156 months (11 – 13 years)	121	101	83.47
>157 months (> 13 years)	66	56	84.84

dramatically. In Ubon Ratchathani, the incidence rate was 25.57, 6.5, 6.7, 10.8, 8.7/100,000 population from 1993 to 1998 respectively[9].

From our study, the measles antibody level at birth was high and then decreased to the unprotective level at age 4-6 months. At 7-11 months of age the antibody disappeared. Infants transplacentally acquired immunity from the mothers who had had measles or measles immunization. The age at which most children lost maternal antibody and the optimal time for measles vaccination varies from 3-6 months in some developing countries to 12 months or later. The rate of loss of maternal antibody is generally inversely related to socioeconomic status[10,11] and results from a combination of factors such as variations in the level of maternal antibodies transferred to the fetus. Genetics and environmental factors determined the differences in the level of placental transfer antibody and catabolism of maternal antibodies in infants[10]. WHO recommended that the measles vaccine should be given at 9 months of age in developing countries, an age at which most infants have lost maternal antibodies and at which seroconversion rate can be acceptably high[12].

The result of our study showed that, after the children received their first dose of measles immunization [Schwarz strain], antibodies increased and then declined to the lowest level at 37-60 months (3-5 years) after immunization or 4-6 years of age. The report by Chunharas from Thailand in 1996 showed that measles antibody declined to the lowest level in about 4-5 years after immunization, after that antibodies rose again especially in children who received the measles vaccine more than 10 years previously. Rising antibody suggested natural immunity[8].

A report by Abdel-Hadi-S et al from Egypt in 1992 showed the seroconversion rate was 85 per cent after Edmonston Zagreb vaccine was given to children 9-11 months old[13]. Data from Thailand by Anantaporn in 1990 suggested that the seroconversion rate was 94.2 per cent after Edmonston Zagreb vaccine was given to children 9-12 months old[8]. Further data from Thailand by Chunharas in 1996 showed that 12 per cent of children who had received the measles vaccine had antibodies lower than the protective level[8]. From our report, the seroconversion rates were 81.1 per cent and 87.1 per cent after the first and second dose of measles vaccine. The seroconversion rate in our report is lower than another report probably due to vaccine failure[14]. Primary vaccine failure occurred in about 5 per cent of the children who were vaccinated at 15 months old, and some showed evidence of waning immunity after vaccination. Primary vaccine failure can be from improperly stored vaccine or route of vaccine administration. Secondary vaccine failure is from poor immune response[14].

From our study, when the children received the first dose of measles or MMR vaccine, 18.9 per cent of them had antibodies lower than the protective level. When they received the second dose, antibodies lower than the protective level were found in only 12.9 per cent of the children. This information showed that the second dose is useful in reducing the number of children who have antibodies lower than the protective level due to vaccine failure. The second dose of vaccine is given to provide a second opportunity to immunize children who missed the first dose and to immunize those who were vaccinated but did not respond to the first dose (primary vaccine failure)[10].

For the purpose of measles control, in addition to the consideration of the earliest possible age for first measles vaccination, increasing vaccine coverage in all age groups, development of more immunogenic vaccine, and revaccination of the second dose after 4 years of age are also recommended. Edmonston Zagreb vaccine given at 4-5 months may provide better protection than the Schwarz vaccine given at 9 months and will solve the problem of contracting measles in children younger than 9 months[13]. The selection of age for the second dose depends on age specific levels of susceptibility to measles and the feasibility of a second contact for vaccination. However, vaccination schedules vary from country to country. In the United States of America, the Committee on Infectious Diseases of the American Academy of Pediatrics [AAP] and the Advisory Committee on Immunization Practices [ACIP] of the Centers for Disease Control and Prevention both recommended a routine second dose schedule of measles vaccine before school entry[18]. A different type of two dose-measles vaccine schedules has been recommended by WHO. In situations in which young infants are at high risk of severe measles, such as in refugee camps and during urban epidemics, it is recommended that the first dose should be given at six and the second at 9 months of age[10].

In Ubon Ratchathani province the highest incidence rate of measles was observed in 0-4 years old children from 1995 to 1998[9]. Data from annual epidemiology surveillance of Thailand showed that, from 1990 to 1994 more than 50 per cent of measles cases occurred among children more than 5 years of age, the highest incidence rate was in the 5-9 year old group but from 1995 to 1998 the highest incidence rate was in the 0-4 year old group[9]. At present, the recommendation of immunization schedule in Thailand is to give the first dose of measles immunization at 9 months and the second dose at 4-6 years of age. From our data, the first dose of immunization in our province and areas of measles hyperendemicity should be given in the younger age group. Immunization in the first few months of life is desirable to close the window of vulnerability between the rapid decline of maternal antibodies. More potent vaccine is also recommended to help increase the seroconversion rate in children younger than 9 months. The second dose should be 3-5 years after immunization or at 4-6 years of age because antibodies are at the lowest level in these age group in our province. A report from Chunharas in 1996 recommended giving a booster dose at 4-6 years because the lowest measles antibody is found in this age group[8].

The main objective of measles control activities in South East Asia through the year 2003 is to reduce measles morbidity and death by 90 per cent and 95 per cent respectively, compared with the prevaccine era[17,18]. In Thailand, the plan of action is to prevent measles outbreaks through enhanced surveillance, sustained high routine vaccination coverage (greater than 90%), and targeted supplemental vaccination should be emphasized. The finding from our study and recommendation will certainly support the achievement of the measles control programme.

SUMMARY

In a survey to measure the level of immunity to measles among children in Ubon Ratchathani province, the authors found that the measle antibody was high during the neonatal period and declined to below the protective level at 4-6 months of age, the antibody was negative at 7-11 months of age. The antibody increased with age after the first dose of measles immunization and decreased to the lowest level 3-5 years after immunization or at 4-6 years of age. The second dose of immunization will increase the number of children who have antibodies above the protective level. Based on the finding from this study, revaccination is recommended at age 4-6 years or 3-5 years after the first dose of measle immunization. No statistical difference of measles antibody between boys and girls in all age groups was found in our study.

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ภูมิคุ้มกันโรคหัดของเด็ก ในจังหวัดอุบลราชธานี

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ได้ทำการตรวจหาแอนติบอดีย์ต่อโรคหัดในเด็กแรกเกิดถึงอายุ 15 ปี ที่อาศัยอยู่ในจังหวัดอุบลราชธานี จำนวน 1,176 ราย โดยวิธี ELISA (Behring Kit) ในระหว่างเดือนกันยายน 2541 – มกราคม 2542 พบว่ามีเด็ก 265 ราย (22.5%) ที่มีภูมิคุ้มกันต่อหัดน้อยกว่าระดับที่ป้องกันได้ (<320 mIU/ml) ในเด็กแรกเกิดพบว่าภูมิคุ้มกันสูงเนื่องจากได้รับภูมิคุ้มกันจากมารดา ค่าเฉลี่ย 6145.16 mIU/ml ในเด็กที่อายุ 4–6 เดือน พบค่าเฉลี่ย 275.83 mIU/ml ซึ่งเป็นระดับที่ต่ำกว่าระดับที่ป้องกันโรคได้ จากนั้นในเด็กอายุ 7–11 เดือนพบว่าระดับภูมิคุ้มกันเป็น 0 ภูมิคุ้มกันจะสูงขึ้นหลังจากได้รับวัคซีนป้องกันโรคหัดครั้งแรกเมื่ออายุ 9–12 เดือน และภูมิคุ้มกันจะลดลงอีกเมื่ออายุ 4–6 ปี หรือ 3–5 ปีหลังจากได้รับวัคซีนป้องกันโรคหัด ในกลุ่มเด็กที่ได้รับวัคซีนป้องกันโรคหัด 2 ครั้ง จะมีจำนวนเด็กที่มีภูมิคุ้มกันต่อโรคหัดสูงกว่ากลุ่มเด็กที่ได้วัคซีน 1 ครั้ง แต่ไม่มีความสำคัญทางสถิติ ผลการศึกษาครั้งนี้ช่วยให้สามารถเสนอแนะได้ว่า เด็กควรจะได้รับวัคซีนครั้งที่ 2 เมื่ออายุ 4–6 ปี เป็นการสนับสนุนตามการสร้างเสริมภูมิคุ้มกันโรคในแผนพัฒนาสาธารณสุข นอกจากนี้ยังพบว่าภูมิคุ้มกันต่อโรคหัดของเด็กหญิงและเด็กชาย ไม่มีความแตกต่างกันในทุกกลุ่มอายุ

คำสำคัญ : ภูมิคุ้มกันโรคหัด, เด็ก, จังหวัดอุบลราชธานี

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