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An Outbreak of Measles in Saitama City, Japan：All Notified Subjects According to an Active Surveillance Program in the Spring of 2007

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Abstract：Measles is considered to be a major health problem worldwide with nearly 35 million cases and 1 million deaths occurring each year. The purpose of this study was to analyze an outbreak of measles in Saitama City, Japan. Saitama City Government has performed an active surveillance on measles since 2005 and all clinical-diagnosed patients with measles have been reported from medical institutions. A total of 376 subjects were received between the 14th week (April 2 to April 8) and the 24th week (June 11 to June 17). Two peaks according to age group were recognized：namely, children less than 2 years of age and the adolescents from 15 to 19 years of age. The latter peak was associated with the period of time when the measles-mumps-rubella vaccine had become a social problem. Japan is said to be a developing country regarding the measles vaccination strategy. In addition, no national program against measles has yet been established. Continuous efforts to increase immunization coverage are needed to interrupt indigenous measles transmission. The Ministry of Health, Labor and Welfare should therefore plan and perform a nationwide program to eliminate measles in Japan.

Key words：**Measles, Vaccination, Non-vaccinees, Surveillance, Saitama City**

Introduction

There were an estimated 30 million to 40 million cases of measles in 2000, causing some 777,000 deaths worldwide. Measles thus account for nearly half of the 1.7 million annual deaths due to childhood vaccine-preventable diseases.[1)] This disease can be eliminated considering its exclusively human reservoir, the lack of a long-term carrier state for the virus and the availability of an effective and safe vaccine.[2)] Regarding a prevention strategy against a transmission of measles virus, Japan is, however, recognized as only a developing country.[3)]

Since the introduction of the measles vaccine to Japan in 1966, the vaccination schedule has changed along with the Preventive Vaccination Law which was revised by the Japanese Ministry of Health, Labor and Welfare (MHLW). The national surveillance system defines measles as a sentinel infectious disease and surveys have been made based on reports from sentinel clinics and hospitals (medical institutions). Therefore, not all measles patients are always reported to the Japanese National Institute of Infectious Diseases (NIID) through the public health centers of local governments. As a result, the MHLW cannot accurately

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estimate the number of measles cases and has also not yet been able to eliminate measles in Japan.

Saitama City has a population of 1,200,000 ; 1.8% of the children under the age of 2 years, 15.5% of 15 to 24 years of age. The prevalence of measles antibodies in children is due to either vaccination or exposure to natural infection. We have begun an active surveillance program for measles since 2005 to promote effective and accurate control measures. Measles are reported by all medical institutions in Saitama City. In the spring of 2007 Saitama City Government received a lot of measles reports from medical institutions. We thus experienced the first outbreak of measles in Saitama City. The same active surveillance program has also been carried out by Okinawa Prefecture Government and Sapporo City Government. However, an outbreak of measles in two areas was not reported.

The purpose of this study was to analyze the reported subjects of measles ; and to assess the first outbreak of measles in Saitama City.

Subjects and Methods

Study population

All physicians working in medical institutions in Saitama City who diagnosed measles reported the information on all patients to the Saitama City Public Health Center (S.C.PHC) as soon as possible. The clinical criteria for a diagnosis of measles was defined as at least 3 days of a generalized maculopapular rash, and a fever of 38.0℃ or over, and cough, mucus or pharyngitis. Each physician reports the patient's sociodemographic data and clinical information including the history of measles vaccination. In addition, the physician can request the Saitama City Institute of Health Science and Research(S.C.IHSR)through S.C.PHC to measure an anti-IgM antibody level in any specific case that physician wants to have such a measurement. Informed consent was obtained from all study participants.

The period from January 1 (Monday) to January 7 (Sunday) in 2007 was defined as the 1st week. The reported subjects were grouped together in one week units. We analyzed all reported subjects of measles from the 14th week (April 2 to April 8) to the 24th week (June 11 to June 17). All information on the reported subjects was sent with deleted personnel data to S.C. IHSR from S.C.PHC. Therefore, the data provided to S.C.IHSR include sex, age, history of measles vaccination, and serum samples.

Laboratory methods

Blood samples were drawn into siliconized disposable plastic tubes. The sera were stored at −20 ℃. The serum samples were tested for anti-measles IgM antibody as measured using a commercially available enzyme immunoassay (EIA) kit (EIA Measles IgM, Denka Ltd, Niigata, Japan)and this kit has a sensitivity of 94.9% and a specificity of 100%.[4] All tests were carried out in duplicate. The criteria used for performing and interrupting results were used according to the manufacturer's instructions.

Statistical methods

The distributions of the various characteristics were compared using the χ^2 test. Probability values of less than 0.05 were considered to be significant. All analyses were conducted using the Statistical Software Package for the Social Science (SPSS Inc., Chicago, IL, U.S.A.).

Results

Table 1 shows the number of subjects according to sex and history of vaccination for each reported week. A total of 376 subjects were reported ; including 218 males (58.0%) and 158 females (42.0%). Of all subjects, non-vaccinees were 170 subjects or 45.2% and vaccinees were 123 subjects or 32.7%. No measurable differences were observed in the distribution of the vaccination status between males and females ($p=0.889$). The peak reported week was the 22nd week (63 subjects : 38.1% of vaccinees and 39.7% of non-vaccinees). 69.1% of all reported subjects were concentrated between the 19th week and the 23rd week.

Of the 376 reported subjects, only 13 subjects required the measurement of anti-IgM antibody levels, and 11 subjects (84.6%) were reported between the 16th week and the 18th week. Of 13 subjects, 10 subjects (76.9%) had an IgM-seropositive and 8

Table 1. Number of measles subjects by an elementary according to the study week

Weeks	Date	Sex		Vaccination			Total
		Males	Females	Vaccinees	Non-Vaccinees	Unknown	
14th	April 2–April 8	1	0	0	1	0	1
15th	April 9–April 15	5	3	1	4	3	8
16th	April 16–April 22	12	13	7	16	2	25
17th	April 23–April 29	16	13	8	17	4	29
18th	April 30–May 6	13	10	8	11	4	23
19th	May 7–May 13	35	14	14	19	16	49
20th	May 14–May 20	38	21	18	33	8	59
21st	May 21–May 27	37	19	25	12	19	56
22nd	May 28–June 3	36	27	24	25	14	63
23rd	June 4–June 10	14	19	9	18	6	33
24th	June 11–June 17	11	19	9	14	7	30
	Total	218	158	123	170	83	376

13 subjects were required the measurement of anti-IgM antibody.
11/13 subjects were reported between the 16 week and the 18 week.
10/13 subjects had an IgM-seropositive.
8/10 subjects were non-vaccinees.

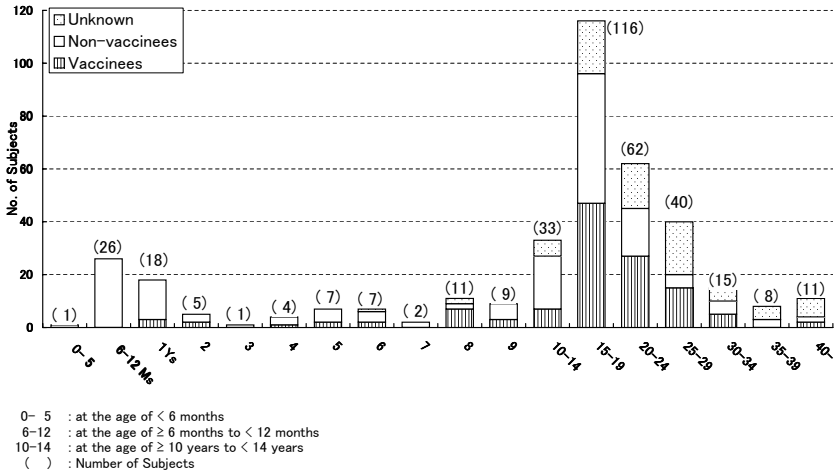

Figure. 1. Number of measles subjects and vaccination by age groups

subjects (80.0%) of them were non-vaccinees.

Figure 1 shows the age distribution according to the history of measles vaccination. The age distribution showed two peaks ; the children less than 2 years of age (45 children : 6.7% of vaccinees and 93.3% of non-vaccinees in these groups) and the young adults around the age of 20 years. The age group from 15 to 19 years was the largest number of reported subjects : 116 subjects or 30.9% (40.5% of vaccinees and 42.2% of non-vaccinees in this group).

Discussion

In the 1980s and 1990s regional or nationwide measles outbreaks have been reported in the Western countries.[5)-11)] Although the incidence of measles has significantly decreased in many countries due to the widespread use of effective vaccines, this disease still causes a significant morbidity in Japan.[3)] The vaccination rate of measles under the age of 7 years is about 90% and that under the age of 2 years is less than 80%,[12)13)] even though the vaccination fee against measles is consistently free of charge in Japan. There are, moreover, no data about the prevalence of antibodies to measles in primary school-aged children evaluated nationwide in Japan.

In April of 2007, the occurrence of measles reported by the national surveillance program has been increasing in the Tokyo metropolitan area and its outskirts including Saitama City. We also

noticed that measles is increasing in accordance with the active surveillance of Saitama City. Only 4 subjects were reported to have measles in 2005 and 22 in 2006 in Saitama City. The measles incidence has thus increased markedly. The fact in the spring is clearly different from the past phenomenon. The first outbreak occurred in our city.

The measles vaccine was introduced in Japan in 1966, and a routine vaccine became the general health care practice since 1978. In addition, measles–rubella (MR) vaccine was introduced since 2006. With respect to measles–mumps–rubella (MMR)vaccine, routine MMR vaccine started since 1989. However, the MMR vaccination program had stopped in 1993, because the side–effect problems including aseptic meningitis induced by a mumps vaccine were reported to develop and the general population thus refused to be vaccinated. This fact that 47.3% of the subjects were in the aged between 15 and 24 years may correspond with the duration that the MMR vaccination being refused. These results suggest that the MMR vaccination failures play an important influence in this epidemic.

Another important problem exists. The Preventive Vaccination Law was revised in 1994：the regulation as the general population ought to receive the vaccination against measles was revised that the regulation as the government encourages the general population to be vaccinated against measles. As results in this study, 12.0% of the subjects were the children under 2 years of age. Almost all subjects (93.3%) less than the age of 2 years was non–vaccinees. This fact definitely suggested that measles vaccination is needed by children under the age of 2 years and the administration should develop a new strategy for this group as soon as possible.

A routine two–dose vaccination has also been recommended in many countries.[11)14)] In 2006, the Prevention Vaccination Law was re–revised as follows;Two–dose vaccination at the age of 12 months to less than 24 months with the measles vaccine or the MR vaccine and at the age of 5 years to less than 7 years with the measles vaccine or the MR vaccine was recommended. The national program should be planned to reach a preventable level with ＞95%[15)] on the seroprevalence of measles antibody in school–aged children.

In 13 subjects, the IgM–seropositive rate was 76.9%. In addition, the date on drawing blood of 2 negative subjects was within 3 days after a rash appeared. It has been well documented that in some cases, antibodies may be seronegative in the early stage of infectious diseases. Therefore, early measles antibody testing may be responsible for the seronegativity of anti–measles IgM antibody in this study. There is, therefore, no denying the fact that the two seronegative samples might be seropositive if blood samples are obtained more than 3 days after a rash appeared. However, only 13 subjects (3.5%) had their anti–IgM antibody levels measured in this study. One of the reasons why the criteria do not include a required antibody test may be a rapid report of clinical diagnosis is more important than an accurate report of laboratory diagnosis about the active surveillance program for measles. Moreover, most physicians do not require the test as they have already obtained information on measles epidemic.

Vaccine–induced antibody titer is lower than naturally acquired immunity[5)] and decrease faster without natural boosting.[16)] It is also reported that maternal immunity resulting from natural infection provides infants with longer protection.[17)–19)] The risk of measles infection is 7.5 times higher in infants born after 1963 than in infants born before 1963 when the measles vaccine was licensed.[20)] The vaccination schedule should be the latest period when most infants lose maternal antibody so that they could be successfully sero–converted, and the earliest period when susceptible infants could be protected from transmission of measles virus.[21)] Moreover, the vaccinees who subsequently develop measles have been reported to have a milder illness than the non–vaccinees,[22)] whereas there were no differences regarding the clinical illness between the two groups.[7)23)] However, a failure of vaccination strategy for measles prevention is going to induce an outbreak of measles in the future.

A nationwide seroepidemiological study that examines the prevalence of antibodies to measles has never been performed in Japan. There is, therefore, no accurate data on the coverage rate. The

lowest sero-positive prevalence in infants is at the age of 9 to 11 months[24] and infants are not protected from measles infection for more than 6 months before receiving a first measles vaccination. If a sero-survey performed by the MHLW obtains the same result, a vaccination schedule on children ≥12 months to <24 months of age must be reconsidered. It is essential that the coverage rate increases and then be maintained at a level above 95%.

It is difficult to estimate the general immunological status in Japan, because it is an expensive and time-consuming process. The MHLW is, however, required to carry out an epidemiological study to elucidate the prevalence of measles antibodies. The MHLW should plan and perform a strategy to eliminate measles. The strategy requires as follows ; maintenance of vaccine coverage above for the first and second vaccination, education of parents with preschool-aged children, and reinforcement of laboratory surveillance for measles.

We evaluated an outbreak of measles in the spring of 2007 in Saitama City. Measles outbreaks signal a failure in the vaccine program. It is required to eliminate the scourge of measles that an immediate implementation of vaccination for all non-vaccinees of children and a complete establishment of routine two-dose vaccination for all preschool children. An increase in the seropositive rate is impossible without an increase in the vaccination rate for preschool-aged children. All mothers living in Japan have a maternity health-record book (Boshi Kenkou Techou). All records of vaccination against infectious diseases about their children are written in the book. Therefore, a mother can recognize whether her child has been vaccinated or not. It is extremely important to increase the coverage rate to practically use a maternity health-record book. The routine two-dose vaccination is effective for the measles control programs since the second dose vaccination is required not only to decrease the small number of primary vaccine failures, but also to boost the immune response. It is, thus, necessary that the two-dose vaccine coverage be over 95% before children reach primary school-age and the seroprevalence of preschool-aged children has to reach the preventable level with at least 95%, because young children are susceptible to measles. To achieve this goal, the unshakable resolve of the Japanese Government is essential.

One limitation of this study was that we could not confirm an IgM-antibody in all subjects in this study. The sero-survey design avoided the indispensable need to take blood samples from pediatric children for the purpose of this epidemiological study. In future studies, there is needed to revise the criteria. An analysis of the genetic characterization of measles virus strains should also be performed in a future study.

Conclusion

In this study, we found an outbreak of measles in Saitama City. Measles vaccination has been regularized at the age of ≥12 months to <24 months and at the age of ≥5 years to <7 years since 2006. However, an outbreak of measles in Saitama City strongly showed that a national program to eliminate measles is needed. This outbreak gave an early warning of the need to reconsider the prevention policy against measles. In addition, parents who have the children under the age of 2 years have to be sure to have their children vaccinated.

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