



## Review Article



# Report of the Korean Society of Infectious Diseases Roundtable Discussion on Responses to the Measles Outbreaks in Korea in 2019

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## ABSTRACT

During the 2019 domestic measles outbreak in Korea, measles occurred in healthcare workers with two doses of the measles, mumps and rubella vaccine, and the strict application of the Occupational Safety and Health Act required medical institutions to identify healthcare workers' immunity to measles and vaccinate the susceptible pockets. In response to the frontline medical institutions' request to review the measles recommendations and guidelines, the Korean Society of Infectious Diseases held a roundtable discussion on the causes of measles outbreak, timing of vaccinations, antibody tests, and booster vaccinations for healthcare workers, and financial support from the government and municipality as well as response strategies against the outbreak in healthcare settings. In Korea, the seroprevalence of measles is decreasing in the vaccine-induced immunity group during

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**Conflict of Interest**

No conflicts of interest.

**Author Contributions**

Conceptualization: YJ, DWP, SHK, HHC, HGJ, SNJ, YHC, EHC. Investigation: SHK, HHC, HGJ, SNJ, YHC, EHC. Validation: DWP, KNK, MJK, JYK, SEP, SYP, BWE, MSL, HWJ, BSC, HJC. Writing - original draft: HS, DWP. Writing - review & editing: HS, DWP, KNK, MJK, SHK, JYK, SEP, SYP, BWE, MSL, HHC, HJ, HWJ, SNJ, BSC, YHC, EHC, HJC, YJ, YSK.

the maintenance of measles elimination over several years. The susceptible group against measles is in their 20s and 30s, and this may be because of waning immunity rather than non-response considering Korea's vaccine policy. The risk of measles nosocomial infection from community increases as these susceptible pockets actively engage in medical institutions. Thus, data on the immunity of low seroprevalence group in Korea are needed, further discussion is needed on the booster vaccination based on the data. Especially, antibody testing and vaccination in healthcare workers may be necessary to prevent the spread of measles in medical insutitutions, and further discussion is needed regarding specific testing methods, and the timing and frequency of test and vaccination.

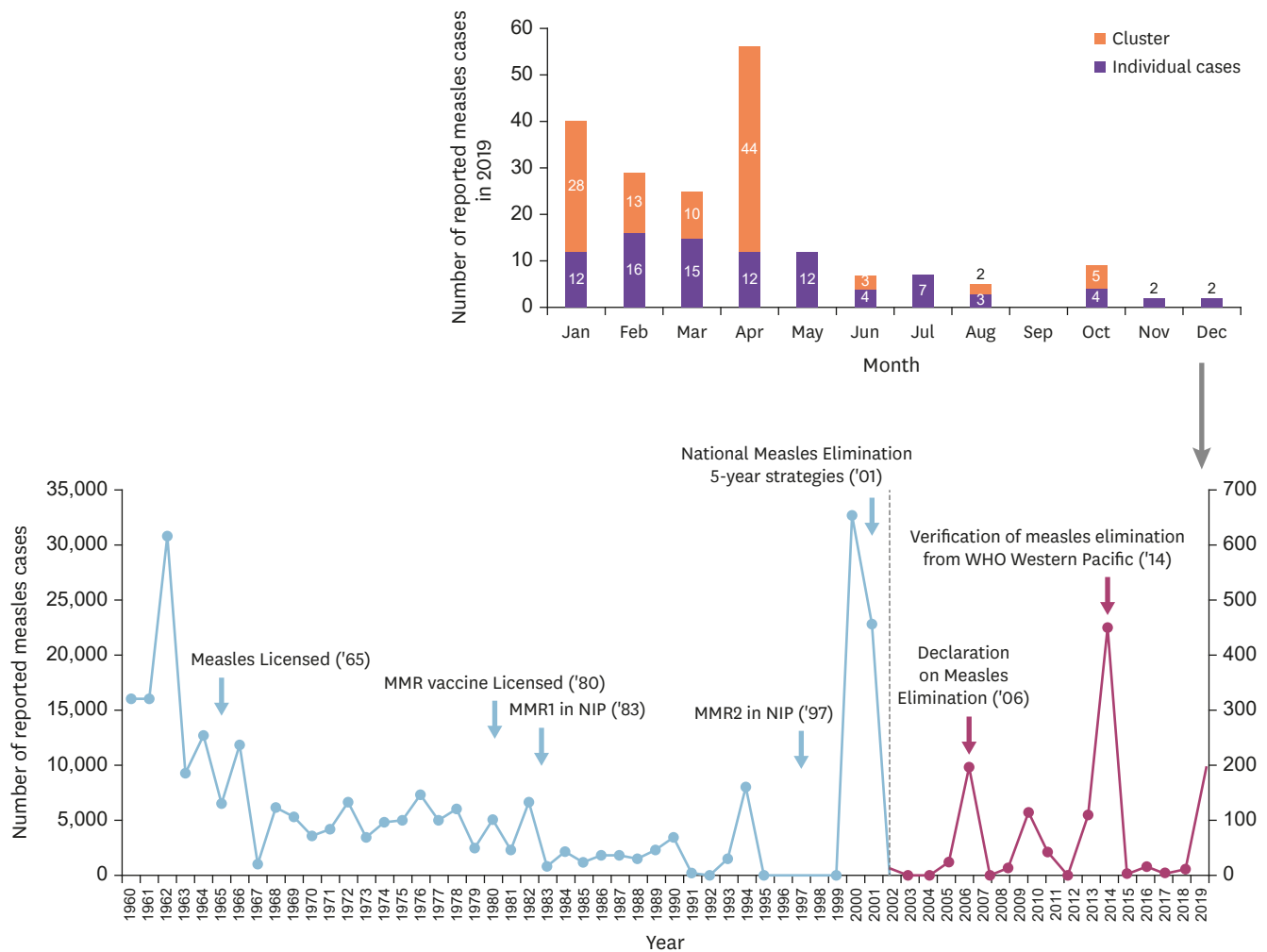
**Keywords:** Measles; Disease outbreaks; Prevention and control; Measles-mumps-rubella vaccine; Vaccines

**INTRODUCTION**

Measles is a highly contagious infectious disease, caused by the measles virus, and, in children, the main symptoms include cough, runny nose, fever, and conjunctivitis, which may be accompanied by respiratory and central nervous system complications. Measles is a vaccine-preventable disease, and the history of measles infection may confer lifelong immunity.

The global morbidity and mortality from measles was high until the first measles vaccine was introduced in 1963 [1]. In Korea, measles had caused serious pediatric morbidity and mortality in pre-vaccine era; up to the mid-1960s, from May to July, approximately one million children reaching about 20 percent of the child population contracted measles and 20,000 of them died (Fig. 1). The first live-virus measles vaccines were introduced in Korea in 1965, and no-cost vaccination program was implemented for the children aged 9 months to 4 years of the poverty group to decrease the measles-related morbidity in March 1970 [1]. The concept of long-lasting protection conferred by two doses of measles vaccination has emerged worldwide in the 1990s. In Korea, the measles epidemic with 4,000–6,000 new cases per year occurred every 4 - 6 years during the early 1980s. In 1985, Korean government implemented no-cost national immunization program that made primary measles vaccination mandatory for children aged 12 - 15 months. In the meantime, the prevalence of measles among 6-year-old children was higher than in the preceding years during the nationwide outbreaks in 1993 and 1994; two doses of the measles vaccination schedule were made compulsory in 1997. Despite these efforts, the 2000 - 2001 pandemic with 52,897 morbidities and 7 deaths occurred. The government established the 5-year National Measles Elimination Plan including, a catch up vaccination targeting 8 - 16 years old population based on national seroprevalence study and the school entry requirement for the certificate of vaccination of the second dose measles containing vaccines. After implementation of the 5-year National Measles Elimination Plan, measles incidence was dramatically reduced to less than one in million people.

Through the implementation of a nationwide survey, a program to confirm a history of secondary measles vaccination, Korea, in November 2006, met the World Health Organization (WHO) criteria for a country that has eradicated measles. Measles outbreaks occurred since 2006, with 194 cases in 2007, 114 cases in 2010, 42 cases in 2011, 107 cases in 2013, and 442 cases in 2014, most of which were imported and nosocomial cases [2-4].



**Figure 1.** Reported cases of measles by year in Korea (1960 - 2019). MMR vaccine, measles, mumps, and rubella vaccine; MMR1, one dose of MMR vaccine; NIP, national immunization program; MMR2, two doses of MMR vaccine; WHO, World Health Organization.

In 2014, Korea firstly received the measles elimination verification certificate from the WHO Western Pacific along with Australia, Mongolia, and Macau, China [5]. While approximately 10 measles patients have been reported annually in Korea from 2014, a total of 194 measles cases have been reported in 2019 [6]. With regard to the route of the infection, 86 individuals (44.3%) had a history of overseas travel and 74 (38.1%) had nosocomial exposure in hospitals. One hundred twenty patients (61.9%) were in the 20 - 39 years age group.

Despite the high vaccination rate, measles outbreaks occurred in various regions in 2019 [7, 8]. In particular, healthcare workers who had received two doses of the measles, mumps and rubella (MMR) vaccine subsequently contracted measles. The strict application of the provisions of the Occupational Safety and Health Act, which stipulated vaccination and identification of healthcare workers' immunity to airborne infectious diseases, required a review of the existing measles management guidelines by frontline medical institutions. Herein, the Korean Society of Infectious Diseases (KSID) held a roundtable discussion on July 11, 2019 to review the current measles management guidelines and to discuss on future direction for infection control and prevention strategies; participants of the KSID meeting is shown in **Table 1**.

**Table 1.** Participants in the roundtable discussion

**President, The Korean Society of Infectious Diseases**

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**Moderator**

Dae Won Park (Division of Infectious Diseases, Department of Internal Medicine, Korea University College of Medicine)

**Panelist**

Sung-Han Kim (Department of Infectious Diseases, University of Ulsan College of Medicine)

Hyun-Ha Chang (Division of Infectious Diseases, Department of Internal Medicine, Kyungpook National University School of Medicine)

Hyungul Jung (Korea Disease Control and Prevention Agency)

Soo-Nam Jo (Infectious Disease Control Center in Gyeonggi-do)

Young Hwa Choi (Division of Infectious Diseases, Department of Internal Medicine, Ajou University School of Medicine)

Eun Hwa Choi (Division of Pediatric Infectious Diseases, Seoul National University College of Medicine)

**Questioners/Commenters**

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Jeong Yeon Kim (Division of Infectious Diseases, Department of Internal Medicine, Sahmyook Medical Center)

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**Report Writing**

Hyeri Seok (Division of Infectious Diseases, Department of Internal Medicine, Korea University College of Medicine)

## VERBATIM MINUTES OF THE KSID MEETING CONDUCTED ON JULY 11, 2019

**Youngmee Jee:** From the end of 2018 to the first half of 2019, the measles outbreaks in Korea were centered on hospitals, raising many questions about whether healthcare workers should undergo measles antibody testing and receive booster vaccination with the measles-containing vaccine (MCV). Today, there will be a discussion with experts on the problems associated with the outbreak response in the field and the response process itself. I hope that the discussion will serve as an opportunity for us to create a consensus on measures to prevent future measles outbreaks.

### 1. What are the causes and problems that caused measles to reappear globally, including in Korea?

**Dae Won Park:** Let's start by discussing the causes and problems in the global and domestic epidemics of measles. First of all, could Hyungul Jung provide an overview of the outbreaks?

**Hyungul Jung:** A worldwide measles epidemic is a current problem. According to a WHO report, by May 2019, there were nearly 2.23 million measles cases, which is approximately three times higher than the incidence of measles in the same period in previous years. In Korea, only 10–20 cases have been reported since 2014; however, from December 2018 to July 2019, 9 cluster outbreak cases were reported. Individual cases involved overseas travelers; Vietnam and the Philippines accounted for approximately 50% and 30% of the cases, respectively.

**Hyun-Ha Chang:** As the state of measles elimination in Korea lasted for more than 10 years, I think that a kind of insensitivity toward safety requirements has occurred. In order to maintain the elimination state, academics have suggested that a strategy that requires healthcare workers to regularly check their immunity and get vaccinated is necessary.

However, governmental policies and communication with the hospital management that are need for this strategy to be reflected in clinical practice are often not implemented. In fact, even when the measles outbreak in Daegu began, antibody testing for all healthcare workers were not routinely performed, and economic support from local governments was not promptly provided.

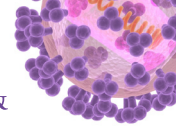
Furthermore, during the actual measles outbreak, the infectious diseases physicians must communicate with the hospital management and other clinicians as the chief of the infection control team. During the strict implementation of infection control guidelines for medical institutions by the quarantine authorities, it was difficult to take responsibility for practical difficulties (*e.g.*, the absolute shortage of healthcare workers due to the post-exposure work restrictions of healthcare workers who are susceptible to measles).

**Soo-Nam Jo:** Gyeonggi-do experienced the highest number of cases during this measles outbreak. The difficulty in responding to the measles outbreak was due to the lack of prior experience in response. The existing manual was not updated, and the the government was unfamiliar in the actual process of application. As the members of the local government are not medical professionals, it seems that the lack of clinical understanding of the disease led to an overreaction to the first outbreak that we encountered. During the course of the outbreak, more experience was accumulated, and this seemingly improved the clinician's proficiency in responding to cases that subsequently occurred. I think it is important to share clinical experiences, and it is necessary to consider how best to share such experiences with local governments and healthcare facility.

**Hyun-Ha Chang:** During the measles outbreak, the guidelines for infection control, which were well applied within healthcare facilities, seemed to be limited when applied in the local community. For example, when interacting with a suspected cases of measles, all healthcare workers wear appropriate personal protective equipment within a healthcare facility; however, when the patient returns to the community, it is difficult to communicate such information or provide protection to exposed individuals without the appropriate protective equipment (*e.g.*, when a patient takes a taxi to go back home, and the taxi driver needs to be informed of the potential exposure). In the case of measles, the exposed person is at a much lower risk if vaccinated, and thus, it is necessary to consider the level of measles management in Korea.

**Young Hwa Choi:** Although Korea has met the criteria for measles elimination, I think that measles epidemic may occur in Korea at any time for the following reasons. First, the Korean population has become diversified due to the increased number of multicultural families; moreover, migrant workers may induce measles epidemics in the local community. For school-age children from these backgrounds, MMR vaccination and boosters, which should be administered during infancy, are possibly not being adequately administered and, indeed, some individuals aver that they have not been vaccinated. When entering elementary school, the possibility of overestimation of the 97% rate of two doses of vaccination in the certificate or the immunization record should be considered. Second, with regard to a measles epidemic in a healthcare facility, it may be necessary to check the measles immunity of healthcare workers. Currently, the prevailing opinion is that individuals born after 1985 (the age group that is currently active at medical institutions) are the generation that received the measles vaccine under the national no-cost vaccination program; however, this inference is based on the vaccination rate and not on the confirmation of immunity. In order to prevent a measles epidemic in Korea, it is necessary to secure immunity in local communities and medical institutions.





**Eun Hwa Choi:** Although the national immunization program for measles was introduced in 1985, the data in the national immunization registry has not been verified by the government until 2011 when the government reimbursed the vaccination cost to medical institutions. Therefore, before 2011, vaccine coverage rate was likely to be estimated based on a doctor's note or personal immunization records rather than the data in the national registry. From a previous study on the birth cohort of 2012, coverage rate of the second dose of MMR vaccine was 60 - 70% [9].

For the community management of measles, the country needs to identify the pockets of unvaccinated individuals and vaccinate them. In fact, the outbreaks in Daejeon and Ansan were due to an unvaccinated cluster, and it seems that the government had an opportunity to manage the unvaccinated cluster as a specific religious group or a specific residence.

**Hyungul Jung:** I agree that the Korean population has become heterogeneous. Migrant workers, international students, and multicultural families contribute to the current measles outbreaks. Currently, the system allows no-cost vaccinations at public health centers using alien registration numbers, although it is uncertain whether this system is being utilized well. The system with regard to foreigners needs improvement, and measures for this are currently in the consultation stage based on the need for consultations with the immigrant department and the Korea Disease Control and Prevention Agency (KCDA).

In the case of medical institutions, the healthcare workers themselves need to come to a consensus to prepare for the measles epidemic. In fact, in the case of measles outbreaks in various regions of Gyeonggi-do, it was identified that the duration of outbreak was shortened if a prompt response was initiated at the time of occurrence of the index case.

## 2. Are there any considerations for vaccine efficacy or vaccination interval in regard to the current measles outbreak despite the high vaccination rate?

**Dae Won Park:** In the case of a measles outbreak occurring despite the high measles vaccination rate, I would like to ask Professor Hyun-Ha Chang whether there are any considerations with regard to the efficacy or timing of vaccination.

**Hyun-Ha Chang:** The antibody positivity rate was low among healthcare workers born between 1994 and 1998, as determined from the data of the Kyungpook National University Hospital during the Daegu outbreak. The population in this age group actively engages in medical practice in healthcare facilities, and a customized approach is needed that considers whether the low antibody positivity rate is attributable to the primary or secondary vaccine failure (PVF or SVF, respectively), assuming high vaccination rates.

**Sung-Han Kim:** With regard to the immunity against measles, I have a doubt about the grand principle of "if you get two doses of MCV, you will maintain your immunity for the rest of your life." As mentioned by Professor Hyun-Ha Chang, at the Asan Medical Center in Seoul, the measles immunoglobulin G (IgG) positivity rate in 1995 was identified as 40% using enzyme-linked immunosorbent assay (ELISA). This is consistent with the data from Kyungpook National University Hospital and the entire domestic data [10-12]. It is necessary to interpret the phenomenon of declining immunity in individuals born after 1995. I hypothesize the existence of a waning-immunity cohort, with rapidly declining immunity, wherein it is necessary to distinguish between PVF or SVF, and the management should be modified accordingly and different approaches should be undertaken. Furthermore, it is necessary to

validate immunity against measles by using different methods, such as the avidity index or measurement of the IgG: IgM ratio 1 month after vaccination.

**Min Ja Kim:** I would like to share my recent measles case. A Vietnamese individual who has a Korean spouse visited the hospital with a rash developed just after returning from Vietnam. She had contacted her younger sister who resides in Vietnam and developed skin rash a few days before. Her measles antibody tests showed, the IgM antibody ratio was 2 AU/mL (positive  $\geq 1.10$ ), and the IgG level was confirmed to be higher than 300 AU/mL (positive  $\geq 16.5$ ). In this patient, acute measles was confirmed through a polymerase chain reaction (PCR) test of throat swabs. Her skin rash almost disappeared within 5 days; this course was faster than that of patients with typical measles. This case might imply a case of natural post-exposure immunity boosting by the infection when the pre-existing immunity waned.

**Eun Hwa Choi:** In the case of those born in 1995, the immunization rate of two doses of MCV administration will be nearly 100%. Compared to those in older age groups, individuals of this age group may not have the boosted immunity by the natural exposure from circulating measles virus because these individuals never experienced measles outbreaks. The comparison of the IgG antibody titers in the 2010 and 2017 cohorts showed lower antibody titers in the 2010 cohorts than those in 2017. In general, it is natural for vaccine-induced immunity to wane with time. Therefore, it is important to determine whether a third dose of the vaccine should be administered to the entire population in the absence of an epidemic in the waning-immunity age group or vaccination should be administered only to high-risk groups, including healthcare workers. In addition, when administering the vaccine to healthcare workers, it is necessary to decide whether to administer the vaccine at the start of their career or during an outbreak. Evidence-based studies are needed to support these decisions.

**Hyungul Jung:** The seroprevalence of individuals born since 1995 shows a different trend depending on the region [13]. In Gyeonggi-do, the antibody-positivity rate among individuals in their 20s was more than 80%. Measles morbidity was 1.5 times higher in women than in men. The cause of this phenomenon may be due to high ratio of women among nursing profession or guardians of infants. Moreover, the fact that Korea has been administering MMR vaccination to the military since 2011 should be considered, and this vaccination in the military may correspond to a third dose of MCV.

It is necessary to redefine the basic reproductive number ( $R_0$ ) value of an epidemic in a measles elimination country. In fact, when reviewing outbreak cases, there would be instances where PCR confirms a measles infection following exposure to measles despite the presence of IgG antibodies. An asymptomatic patient was diagnosed with measles on PCR testing in spite of a clear history of having been administered two doses of MCV administration, which is used to define immunity against measles. Furthermore, it is necessary to consider the infectivity of these patients. In actuality, the above mentioned patient had no history of a secondary attack.

**Hye Won Jeong:** I suggest considering the possibility that compliance may increase if the timing of the second dose of MCV is set at a lower age than 4 - 6 years.

**Eun Hwa Choi:** According to the results of the seroprevalence of measles in Korea to date, the immunogenicity is maintained well between the first and the second vaccination doses (12 months and 4 - 6 years of age, respectively) [14]. One concern is that we observe that the level

of Ig G titers waned over time; therefore, the benefit of advancing the second vaccination dose to an earlier timepoint would not be great. Rather, in terms of the schedule, as there are two vaccines (DTaP-polio vaccine, MMR) that need to be administered at 4 - 6 years of age, vaccinating at the same timepoint is a good strategy that can increase the vaccination rate.

**Sung-Han Kim:** According to the Quebec epidemic report, those who received the first dose at 12 months of age had significantly higher susceptibility to measles compared to those who received the first dose at 15 months, which I believe is related to immature immunity [15]. It is also necessary to consider administering the first vaccination beyond 12 months of age.

**Eun Hwa Choi:** Although there is a report that the antibody conversion rate is actually better at 15 months than at 12 months, we should consider the susceptibility to measles of young infants [16]. I do not think that it is a good idea to extend the vulnerable period beyond 12 months of age because infants have nearly 0% maternal antibody at the age of 12 months [17]. Delaying vaccination to address the problem of waning immunity in the future, which can be explained by immature immunity of infants may have some benefits, however, it is important for pediatricians to vaccinate susceptible young infants, who do not have maternal antibodies.

**Hye Won Jeong:** Efforts to validate the ELISA method should also be considered. Most of the ELISA testing is specified based on the serotype A vaccine strain; however, it is necessary to consider whether the recently prevalent serotype is included in the tests [1].

**Hyun-Ha Chang:** A paper published in Iran reported that the antibody titer of Serotype B3 was lower than that of other serotypes in the plaque reduction neutralization test (PRNT) [18]. Serotype B3 was the prevalent type in Daegu; therefore, I wondered whether a low antibody titer that was specific to this serotype may be an underlying reason for the prevalence of this serotype.

### 3. Is antibody test for measles necessary for healthcare personnel regardless of vaccination history?

**Dae Won Park:** In this outbreak situation, many healthcare facilities conducted measles antibody tests among healthcare workers, and the directors of infection control have been concerned about the range of subjects to be tested. Let's discuss whether the antibody tests are necessary for healthcare workers regardless of their vaccination history, which group it should be administered to, and whether periodic testing is necessary.

**Hyun-Ha Chang:** I think antibody testing is required for all healthcare workers until a definite vaccination history is identified because the current problem is that the vaccination history cannot be confirmed with certainty. Thus, vaccination history should be determined from immunization records maintained through the National Immunization Program (NIP).

**Sung-Han Kim:** In Asan Medical Center, an overall investigation for measles has been conducted since 2019 among the employees, including contract workers such as sanitary workers and security personnel as well as full-time workers. According to the study, if the antibody positivity rate is less than 85 - 87%, then the cost-effectiveness of MMR vaccination without conducting an antibody test is high [19]. Accordingly, it may be a better option for employees aged 25 - 30 in Korea to receive MMR vaccination without antibody testing. Although our hospital conducted the antibody tests while contemplating whether to vaccinate or test for measles, it may be a reasonable option to vaccinate without testing.



**Se Yoon Park:** If the MMR vaccination is given without antibody testing, it should be considered that under-vaccination against rubella or mumps may occur. Therefore, rubella and mumps antibody testing may be considered simultaneously with measles antibody testing.

**Young Hwa Choi:** The third dose of MMR vaccination in the military was undertaken because of mumps, not measles, and it is known that a single dose of MMR vaccination is sufficient to maintain immunogenicity against rubella [20, 21]. Therefore, it is reasonable to perform only antibody test for the measles to decide whether to administer the MMR vaccine based on the test result.

**Eun Hwa Choi:** I think it is better to test for the measles antibody in the age group without a reliable vaccination history. I do not think that antibody testing is necessary for all age groups. I don't think there is any need to conduct antibody testing in the age group where the antibody-positive rate is already more than 90%. Further discussion is needed on the cut-off for the age group that requires antibody testing.

**Hyun-Ha Chang:** Amid the measles outbreak in Daegu, there was no time to wait for the results of antibody testing; therefore, MMR vaccination was performed without antibody testing. In fact, if no antibody test is conducted, a problem may arise wherein the disposition of healthcare workers during the measles outbreak would need to be judged by the vaccination status rather than the antibody titer.

**Hee Jung Choi:** I think it is necessary to complete measles vaccination in people with negative antibody test and to perform an additional antibody test following vaccination. In fact, in one case, equivocal and negative results were confirmed when healthcare workers who had undergone vaccination at the hospital underwent an IgG antibody test during the measles outbreak. Even after healthcare workers have completed the measles vaccination schedule, it is necessary to check the postvaccination baseline antibody titer because an outbreak of measles can recur in a medical institution at any time. Furthermore, even if the baseline antibody titer is measured, the question remains whether the antibody titer at 3 or 5 years after vaccination confers a protective effect against measles.

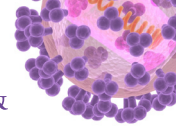
**Jeong Yeon Kim:** The question is whether it is possible to judge that individuals in the general public, and not a healthcare worker, who are exposed to a high-risk group have sustained immunity with two doses of vaccination. The current measles management guidelines in Korea suggest that additional antibody testing is not required even in high-risk groups if the administration of two doses of vaccination is confirmed [22].

**Hyungul Jung:** From the perspective of government agencies, when 5,000 to 7,000 contacts occur during the outbreaks, immune status is evaluated based on vaccination history regardless of high-risk group because of too many numbers of contacts. In high-risk patients, additional antibody testing may be a good option.

#### **4. Do healthcare personnel need additional measles vaccinations?**

**Dae Won Park:** Now let's talk about boosting the MCV to healthcare workers.

**Hyun-Ha Chang:** Whether booster vaccination should be given to healthcare workers who test negative for measles antibodies depends on whether they are PVF or SVF. However, at the present time, there are insufficient data on whether the low immunity problem of this



specific age group is PVF or SVF, and background study regarding this issue is necessary. In addition, there are insufficient objective data on whether vaccination is necessary when the antibody titer is waning. Since the 1990s, studies have been conducted to survey whether re-vaccination is necessary to healthcare workers who have the reduced antibody level after 2 dose-MMR, and suggested that revaccination might be necessary for medical personnel with reduced antibody levels to prevent nosocomial transmission of measles [23-25]. In these patients, it is necessary to confirm whether vaccination is actually necessary through tests such as the PRNT.

**Eun Hwa Choi:** Vaccine-induced immunity is waning, although this does not necessarily mean SVF. A negative result on antibody testing conducted several years after vaccination does not define vaccine failure. Of course, there is a concern that SVF may occur because of the rate of waning immunity increases with the time from the vaccination. As the antibody test was originally designed for the purpose of detecting antibodies generated after natural infection, the test may not detect vaccine-induced antibodies. Among those who have negative results on antibody tests, many people may be able to mount a defensive immune response based on immune memory within a few days if they are exposed to measles. Therefore, I do not agree that all 60% of those who test negative on the IgG antibody test will have vaccine failure.

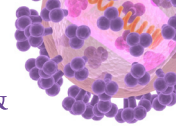
**Young Hwa Choi:** It should be flexibly accepted that 3% of non-responders emerge even after receiving two doses of MCV administration. Thus, there are bound to be susceptible individuals in healthcare facilities, and I wonder whether too much money and resources are being invested due to the sporadic occurrence of one or two such patients. If quarantine for measles is implemented similarly as for Middle East Respiratory Syndrome (MERS), the consequent utilization of manpower and medical expenses would become excessive.

**Hyungul Jung:** Some healthcare facilities have a strategy giving priority to vaccinate susceptible individuals in high-risk departments, then non-medical staff may be excluded from vaccination. Instead of this strategy, it is necessary to vaccinate all susceptible workers regardless of department. In the actual epidemiological investigation of the measles outbreak, if the exposure period is long, it would be difficult to trace the close contacts and, as the transmission period of measles is long, secondary infections outside the expected range may occur.

**Min Ja Kim:** When the vaccination rate reaches approximately 95%, considering the  $R_0$  value of measles, when an index case of measles occurs, it does not progress to an outbreak, but appears sporadic and disappears. Thus, susceptible individuals should be targeted for vaccination.

**Sung-Han Kim:** I agree that vaccination should be targeted at pockets of susceptible individuals in their 20s and 30s, and I think that these individuals should be evaluated only by the antibody titer, and not the vaccination history.

**Youngmee Jee:** In relation to the 2019 measles outbreak, tests including PRNT and avidity testing are ongoing. According to data from the United States, 10% of the infected patients were vaccine failure, and there were cases where the PRNT titer was high in cases with measles [26]. Therefore, determining the target of vaccination based on the antibody titer is not a perfect strategy. Personally, I think it would be better to administer MCV without testing in susceptible age groups, although this should be decided based on an objective analysis of



the data. “Measles reinfection” is a new term that was defined by the WHO working group. In other words, it is believed that measles reinfection may occur. Receiving two doses of vaccination ensures that vaccination for measles is complete.

**Byung Wook Eun:** In Taiwan, “firstline medical personnel” were selected during the measles epidemic [27], and staff from the department of pediatrics, emergency room, infectious diseases, respiratory medicine, etc. were prioritized. This strategy of performing using more concentrated resources, such as antibody testing and immunizations, as needed in the high-exposure group, and tapering it down in those who are expected to have relatively low contact can be advantageous for conserving resources.

**Kwang Nam Kim:** I would like to share details of a case of in-hospital transmission that became an index case last December when an outpatient nurse went to Southeast Asia for overseas volunteer work. The nurse had an atypical presentation, with a non-typical rash and Koplik spots on the tonsils. When the number of exposed individuals was counted, more than 1,000 people had been exposed and all of them could not be vaccinated. Therefore, only high-risk departments were selected for antibody testing and vaccination. Subsequently, in March, a resident was infected by a patient in the emergency room, and by tracing the record of this resident, many secondary infections, including among laboratory staff, clinical trainees, and hospitalized patients, were detected. Again, antibody testing was conducted for all employees, and individuals who had negative results for test were excluded from working at the hospital, which made it difficult to support healthcare workers in the hospital. In view of such cases, antibody testing for all employees from the beginning of the outbreak may be a better option.

At that time, approximately 2,000 people underwent antibody testing, and 180 people were confirmed to have negative results. Following the first vaccination, the antibody test was confirmed to be negative in 10 people and, therefore, a second vaccination was administered.

**Young Hwa Choi:** It is thought that the third vaccination can be helpful during the epidemic. However, a limitation is that no one knows for how long the immunity can be maintained through additional vaccination.

**Sung-Han Kim:** Individuals who do not currently have an antibody titer but have been confirmed to have been vaccinated (considering the measles vaccination project in Korea, it will be difficult to find individuals who are not vaccinated) can be divided into two categories: non-responders which is classified into PVF or individuals with partial immunity, which is secondary to a possible waning of immunity. In the case of a non-responder, I think that two doses should be administered; however, in the case of an individual with waning immunity, I wonder whether two doses of vaccination are needed. It cannot be determined whether an individual is a non-responder or is experiencing a waning of immunity because of the unavailability of data in Korea, such as the IgG:IgM ratio, avidity index, or PRNT. Considering the vaccination history, the infection is thought to be mostly waning of immunity; moreover, in this case, one additional vaccination should be sufficient.

**Soo Eun Park:** I am also in favor of Professor Sung-Han Kim's statement that a single booster vaccination is sufficient. People in their 20s and 30s think that they have received the measles vaccine at least once before, and I do not think that there are really any data on whether these individuals have been vaccinated twice. In addition, the concept of a difference of  $\geq 4$  weeks

between live vaccines was previously lacking. Thus, in Professor Sung Hee Oh's paper in 2014, the incidence of the inappropriate interval between the varicella and MMR vaccinations was as high as 20 - 50% [28]. Perhaps, the abovementioned inappropriate interval between vaccinations may have contributed to the partial immunity to measles among individuals who are in their 20s and 30s.

**Eun Hwa Choi:** I agree that the possibility of waning immunity is high in people in their 20s and 30s because there is a high probability that they have already received MMR at least once in Korea, and I agree that one additional dose may be sufficient. The idea of administering another dose to a person without antibodies against measles seems to be more appropriate than the idea of administering the third and fourth booster doses to a person who has been confirmed to have received the booster dose twice. In Korea, where vaccination history is not objectively specified, the antibody titer may increase among those who do not have the antibody. In contrast, we do not know the effect of the third booster dose in those who have already received the second dose but did not produce antibodies or in those who have waning antibody titers.

**Dae Won Park:** An employee who has definitely been vaccinated twice but has a negative result for antibody test is concerned about whether it is safe to treat measles patients and whether post-exposure prophylaxis (PEP) is necessary after exposure.

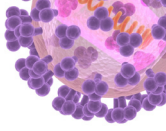
**Eun Hwa Choi:** Hypothetically, these individuals have immunity; however, healthcare workers should wear appropriate personal protective equipment when they care patients having measles, as definitive vaccination and antibody positivity does not incontrovertibly indicate complete immunity against measles. For the same reason, PEP should be undertaken in situations where there is exposure.

### 5. What is the central and local government's policy on financial support for antibody testing and active or passive immunization during the outbreak in the healthcare setting?

**Dae Won Park:** During the measles outbreaks, there were concerns about the cost of testing and active or passive monitoring for high-risk individuals and exposed individuals in healthcare facilities as well as in the local community, and there were differences in policies with regard to this issue among hospitals and among regions. Let us discuss it, starting with Soo-Nam Jo.

**Soo-Nam Jo:** It should be considered separately, depending on whether there is a measles outbreak, and I think that financial support can be provided during the epidemic. However, such financial support is not uniformly provided and is possible only with the will of the local government, through close communication between each local government and the healthcare facility. In this outbreak, Ansan city is a representative case where financial support was provided by local governments. This support can be extended to other infectious diseases besides measles, and financial support was provided for the current hepatitis A epidemic. Moreover, the central agencies of the country are discussing how these policies for financial support can be applied to other infectious diseases.

**Hye Won Jeong:** During an in-hospital measles outbreak, it is difficult to carry out both antibody testing and vaccination if the contacts are not employees or healthcare workers. I think that support from government agencies may be needed in this area.



**Mi Suk Lee:** If the high-risk patients, such as immunocompromised patients or pregnant women, are exposed to measles patients and their immune status is unclear, then the administration of intravenous immunoglobulin (IVIG) should be considered in the PEP. IVIG administration costs approximately 1 million won per person, and there are questions whether it is right for the healthcare facility to cover all the costs. I do not think that it is reasonable for a medical institution to fully cover the responsibility when a community infection enters a medical institution.

**Hyun-Ha Chang:** In fact, there was no financial support for IVIG prophylaxis for pregnant women in Daegu during the outbreak, and the antibody test could not be conducted for all exposed individuals; therefore, IVIG was administered to pregnant women without antibody testing, and all expenses were covered by each healthcare facility. In the case of Kyungpook National University Hospital, the overall IVIG cost was approximately 10 million won.

**BumSik Chin:** If a medical institution administers expedited group vaccination to its employees during epidemic situation, there is a possibility that the vaccination record would not be registered to the KDCA website because the registration process itself maybe time consuming. Therefore, in order to maximize the fidelity of vaccination history of healthcare workers in KDCA registry, it would be better to establish a route to collectively register the vaccination history of medical personnel to KDCA during the outbreak situation.

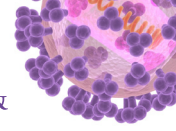
## SUMMARY

In Korea, which was certified by the WHO in 2014 as a measles elimination country and where measles elimination has been maintained so far, measles outbreaks occurred and involved 194 people in 2019; the KSID conducted a roundtable discussion in this regard. After the 2001 pandemic, as the measles elimination status in 2006 was maintained for more than 10 years, both medical staff and government agencies had developed a diminished alertness to the measles epidemic situation. Although there is an opinion among infectious disease specialists that healthcare workers should be regularly evaluated to ascertain immunity and be vaccinated, there were difficulties in aligning the communication between the hospital management and the governmental policy.

The approach to measles epidemic prevention should largely consist of measures to prevent the spread of measles to the community and healthcare facility. In the case of the local community, unlike earlier, the proportion of Korean citizens who are unvaccinated against measles is increasing due to the increasing number of migrant workers, international students, and multicultural families. In the case of healthcare facilities, healthcare workers in their 20s and 30s, who are active in healthcare facilities, did not previously experience a measles epidemic; therefore, these individuals constitute the generation that did not experience natural immunity boosting against measles. In this age group, the seropositivity rate of measles is actually lower than that of the other age groups, and PVF or SVF must be considered as possible reasons for the low positivity rate. In case of a measles epidemic within a medical institution, close communication and economic support from government agencies may be required for rapid outbreak management.

In 1985, the national no-cost MMR vaccination program was introduced and, from 1994 onwards, it was mandatory to submit a certificate of the second MMR vaccination when entering elementary school. Soldiers entering the military after November 2011 received an





additional dose of the MMR vaccine. Therefore, there is a high probability that individuals born in 1985 or later have received at least one MMR vaccination. Basically, in the case of vaccine-induced immunity without natural boosting, waning immunity, wherein the antibody titer decreases, is a natural phenomenon. Exposure to measles at this age means that, even if a previous vaccination has taken place or antibodies are present, atypical measles or a weak infection may develop; moreover, a negative antibody titer does not necessarily mean that the person is susceptible to measles and can be protected by immune memory. It is unknown whether the decrease in antibody levels in this age group is due to PVF or SVF, and further research is needed into this area. Therefore, in addition to simply measuring IgM or IgG levels through ELISA, it may be necessary to evaluate immunogenicity against measles through tests, such as the avidity test, PRNT, and IgG/IgM ratio.

The necessity of antibody testing and MCV administration for those born after 1985 in medical institutions remains under consideration. First, in the case of antibody testing, there is no clear set of criteria on whether and when to check for the presence of antibodies for measles epidemic prevention among workers at medical institutions who are in their 20s and 30s. Some individuals argue that MCV administration without antibody testing may be cost-effective. However, during a measles epidemic, it may be necessary to conduct an antibody test in advance for medical staff assignments and to test for antibody titers, preferably among all employees in the cluster of the susceptible age group, although not among those in high-risk departments. There is controversy about the periodic update of the antibody test. Secondly, there were many opinions on whether the target of the MCV booster vaccination should be based on the results of the antibody test rather than the vaccination history because it is difficult to judge the immunization record based on objective data, as the records prior to 2011 were not recorded through real-time NIP registration. If an individual has a negative result for the measles antibody, a booster vaccination is recommended; however, the number of boosters (one or two doses) to be administered is controversial, and this will depend on whether the patient has PVF or SVF. Although there is no objective evidence, there are many opinions that a single dose may be sufficient because most of these individuals are likely to have SVF with partial immunity, based on the assumption that at least one MMR vaccination has been administered. After vaccination, antibody testing may be repeated to evaluate immunogenicity. In addition, universal MMR vaccination at 12-month should be re-evaluated for one of the various causes of many Korean young adult with waning immunity, and further studies are needed on whether a few months delay up to 15-month may be beneficial to overcome this unique phenomenon in Korea. Considerations in vaccination is to establish a health care provider registry of vaccination record in KDCA, and a simplified procedure, such as batch registration of vaccinations, may help manage medical staff in the future.

In conclusion, while maintaining the measles elimination status, the age group without natural boosting showed naturally decreasing immunogenicity in Korea. The proportion of healthcare workers comprised individuals with increasing susceptibility to measles, and it is necessary to discuss a relatively homogeneous screening protocol and vaccination strategy in Korea. Therefore, objective data on the waning of vaccine-induced immunity in the in the 20s and 30s age group are required. Antibody testing and vaccination for healthcare workers born after 1995 may be needed to prevent the spread of measles in healthcare facilities in Korea in the future.

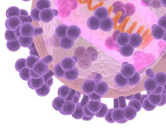
## SUPPLEMENTARY MATERIAL

Korean version

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