



Measles Elimination Activities in the Western Pacific Region: Experience from the Republic of Korea

Young June Choe,¹ Youngmee Jee,²
Myoung-don Oh,³ and Jong-Koo Lee^{4,5}

¹Department of Epidemiology, Seoul National University School of Public Health, Seoul; ²Center for Immunology and Pathology, Korea National Institute of Health, Seoul; ³Department of Medicine, Seoul National University College of Medicine, Seoul; ⁴Department of Family Medicine, Seoul National University College of Medicine, Seoul; ⁵JW Lee Center for Global Medicine, Seoul National University College of Medicine, Seoul, Korea

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Address for Correspondence:

Jong-Koo Lee, MD

JW Lee Center for Global Medicine; Department of Family Medicine, Seoul National University College of Medicine, 101 Daehak-ro, Jongno-gu, Seoul 03080, Korea
Tel: +82.2-740-8992, Fax: +82.2-3668-7367
E-mail: docmohw@snu.ac.kr

We describe the global status of measles control and elimination, including surveillance and vaccination coverage data provided by the World Health Organization (WHO). Since 2000, two doses of measles vaccine (MCV2) became recommended globally and the achievement of high vaccination coverage has led to dramatic decrease in the measles incidence. Our finding indicates that, in the Western Pacific Region (WPR), substantial progress has been made to control measles transmission in some countries; however, the measles virus continues to circulate, causing outbreaks. The Republic of Korea (ROK) experienced a series of resurgence of measles due to the importation and healthcare-associated transmission in infants, however overall incidence and surveillance indicators met the WHO criteria for measles elimination. The ROK was verified to be measles-free along with Australia, Mongolia, and Macau, China in 2014. One of the effective elimination activities was the establishment of solid keep-up vaccination system in school settings. The lessons learnt from the measles elimination activities in Korea may contribute to enhancing the surveillance schemes and strengthening of vaccination programs in member countries and areas of WPR.

Keywords: Measles; Korea; Western Pacific Region; Elimination; Surveillance

BACKGROUND

Measles is a highly contagious disease that infected almost all vulnerable populations during the pre-vaccination era, with the case fatality rate ranging 3%-15% in the developing countries (1). The transmission occurs through droplets or aerosols and results in secondary attack rate of more than 70%-80% in susceptible populations (2). Measles is potentially eradicable because humans are the only reservoir to the virus, a sensitive and specific diagnostic tool is available, and an effective vaccine is available (3).

The vaccines play a key role in the elimination of measles. It is estimated that one dose of measles vaccine confers at least 95% effectiveness in preventing clinical measles and 92% effectiveness in preventing secondary cases among household contacts (4). The highly transmissible measles records basic reproduction number of greater than 10, therefore the vaccination coverage of more than 95% is necessary to achieve effective herd protection from the vaccines (5). Current strategies for the global eradication of measles include achieving high vaccination coverage coupled with epidemiological and laboratory surveillance. The two-dose measles vaccination program is now being recommended globally, however, the implementation is challenging in countries with limited health resources. The weak

health systems hinder the key components in routine vaccination services: stable vaccine procurement, maintenance of cold-chain, and effective vaccination delivery. To overcome these challenges, various vaccination strategies have played a role for attaining adequate vaccination coverage and stopping endemic transmission of the measles virus in the community (6,7).

In the World Health Organization (WHO) Western Pacific Region Office (WPR), substantial progress has been made to control and interrupt measles transmission (8). However, the measles virus continues to circulate causing outbreaks in the WPR countries, potentially due to limited success in achieving universally high vaccination rates at the sub-national level. In this report, we aimed to provide perspectives in measles elimination, with sharing the experiences from the Republic of Korea, to intensify efforts to close gaps in population immunity of measles with the WPR member states and regions.

GLOBAL MEASLES ELIMINATION ACTIVITIES

The measles-containing vaccines (MCV) have been used routinely in many countries, employing different schedules and doses for nearly 50 yr. Strengthening of the measles vaccination activities dates back to the 1974, when the WHO has initiated the Expanded Program on Vaccination (EPI), aiming to develop

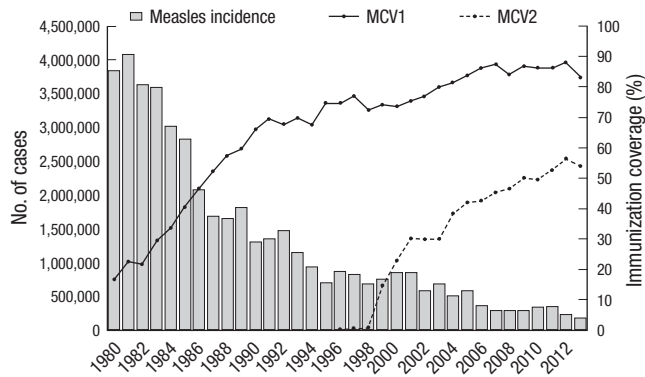


Fig. 1. Global number of reported measles cases and estimate of the first and second doses of measles immunization coverage, 1980-2013. MCV, measles containing vaccine.

and support the increase of vaccination coverage (9). However, the global vaccination coverage in the 1980s was low, less than 60%, and consequently measles continued to prevail causing more than 2 million cases per year. In the late 1980s, following the World Health Assembly's resolution to reduce measles morbidity by 90% and mortality by 95% and the World Summit for Children's implementation to target vaccination coverage among 90% of children, the measles cases decreased to 1-1.5 million annual cases in the 1990s (10). In 2000, the WHO and the United Nations Children's Fund (UNICEF) have recommended the two doses of measles vaccine (MCV2) in every child. Globally, the achievement of high vaccination coverage of the first and second doses of MCV has led to dramatic decrease in the measles incidence (Fig. 1).

However, concerns have been raised over the apparent discrepancies between coverage rates in the WHO Regions. The Regions of Americas and Europe, with their steady increase in the vaccination coverage since 1980, have reached MCV1 coverage of more than 90% in the 1990s, and sustained low incidence of measles in the 2000s (Fig. 2). The increase in MCV1 coverage in Regions of Eastern Mediterranean and Western Pacific were noted in 1980s, but less than 90% coverage in the 1990s led to ongoing transmission of the virus in their Regions. In the Regions of Africa and Southeast Asia, there were significant reduction in overall incidence rates; however, the Region's most remote and hard-to-reach population are still vulnerable to transmission and outbreak of measles due to poor access to vaccines.

ELIMINATION OF MEASLES IN THE REGION OF AMERICAS

In 2002, the Region of Americas became the first WHO region to interrupt measles transmission, and several lessons have been learned from their experiences. Innovative measles vaccination strategies were implemented in the Region since 1990s. The strategies aimed to rapidly interrupt the measles transmission by

performing mass vaccination campaigns, namely "catch-up", "mop-up", and "follow-up", and to maintain high population immunity by providing adequate vaccination coverage to each successive birth cohorts through routine vaccination services (11). The "catch-up" vaccination campaign is a one-time mass vaccination campaign conducted for a defined age group (usually children aged 9 months to 14 yr). After the "catch-up" campaign was conducted, there were portions of the population with inadequate vaccination coverage; therefore a "mop-up" campaign was conducted to increase vaccination in areas of low coverage. Because the vaccine is not 100% effective and the measles virus is highly transmissible, the accumulation of susceptible population over time may result in on-going transmission of the virus; therefore, a "follow-up" vaccination campaign was conducted every 2-5 yr periodically to increase the population immunity.

Between 1989 and 1995, a total of 39 out of 41 countries in the Region of Americas have conducted catch-up campaigns and periodic follow-up campaigns every four years (12). All children aged 9 months to 14 yr, irrespective of previous vaccination history, have been vaccinated within a short period of time. Since there may still remain pockets of population with limited access to catch-up campaign, the special vaccination or mop-up campaign were carried out in areas to increase their level of immunity. The catch-up and mop-up campaigns resulted in a rapid increase in population immunity, and contributed in overall reduction of measles incidence in the Region. After the initial catch-up campaign, strengthening of routine vaccination services to "keep-up" at least 95% of each birth cohorts at 12-15 months of age was conducted. And to ensure the adequate herd immunity among children, the "follow-up" vaccination campaigns had been conducted. These vaccination strategies were accompanied by the improvements in virologic and epidemiologic surveillance schemes.

The implementation of the vaccination strategies in the Region of Americas has resulted in reduction of measles incidence as depicted in Fig. 2. The number of measles cases declined to 537 in 2001; more than 99% lower than previously reported in 1990. Among all WHO Regions, the Americas accounted for 6.6% (185,793 out of 2,794,053) during 1980-1991, while the proportion decreased to 2.6% in 1992-2003, and to 0.1% in 2004-2013. Between the three periods, the incidence rates in the Region of Americas have decreased by 90% and 99%, respectively (Fig. 2, Table 1).

WESTERN PACIFIC REGION AND THE ELIMINATION GAP

Since the 1960s, many countries and areas of the WPR have included MCVs as a part of their routine vaccination program (13, 14). By 1990s, all member states have included measles vaccine,

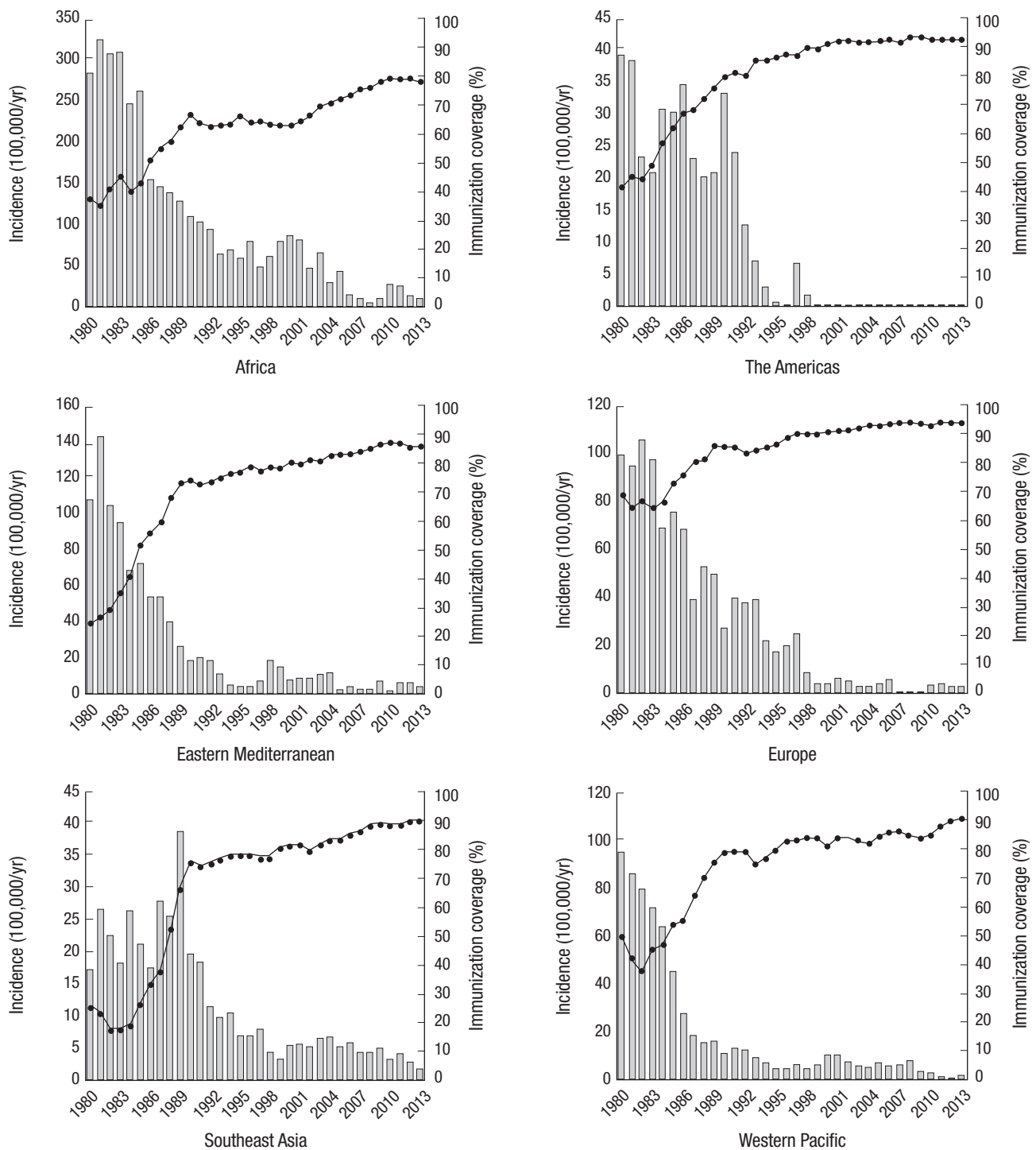


Fig. 2. Measles incidence rate per 100,000 population/year and estimate of the first dose of measles vaccination coverage by WHO Region, 1980-2013. WHO, World Health Organization; incidence, reported case per 100,000 population per year; bar represent incidence rate, line represent immunization coverage.

usually in the form of monovalent vaccine, and in Guam, Hong Kong, Palau, and Singapore, it is given in the form of measles-mumps-rubella (MMR) vaccine. MCV2 was first implemented in American Samoa, New Zealand, Palau, and Samoa. As the poliomyelitis eradication activities have led to strengthening of routine immunization system, it also contributed to increase of

measles vaccination coverage in Cambodia, China, Lao PDR, the Philippines, and Vietnam (15). During the national immunization days for poliomyelitis eradication in the Philippines, supplementary measles and tetanus toxoid vaccines were also given to all children between 9 and 59 months of age (16). By 2003, the introduction of measles immunization programs in

Table 1. Time trend in the estimated incidence of measles by WHO region

WHO region	Estimated incidence per year, n (%)		
	1980-1991	1992-2003	2004-2013
Africa	914,461 (32.7)	425,588 (49.2)	165,650 (44.2)
The Americas	185,793 (6.6)	22,202 (2.6)	273 (0.1)
Eastern Mediterranean	212,790 (7.6)	47,875 (5.5)	28,619 (7.6)
Europe	584,591 (20.9)	141,656 (16.4)	26,653 (7.1)
Southeast Asia	267,540 (9.6)	101,956 (11.8)	75,104 (20.0)
Western Pacific	628,878 (22.5)	126,133 (14.6)	78,602 (21.0)
Total	2,794,053	865,409	374,900

WHO, World Health Organization; incidence, reported case.

WPR countries has resulted in dramatic decreases in morbidity and mortality attributable to measles. In Pacific islands, Australia, Mongolia, and Korea, experiences indicate that elimination can be achieved in countries with diverse geography, populations, and measles epidemiology (13). Between 1980 and 1991, the estimated annual incidence in the WPR was 628,878 cases, which accounted for 22.5% of the global incidence (Table 1). The number of cases per year from 1992 to 2003 decreased to 126,133 cases, and further down to 78,602 cases in 2004-2013.

The strategy used in the WPR in 1990-1995 was to “control” measles; in 1996-2002, was to “accelerate control”, and from 2003 to now, “elimination” (17). In 2005, the 37 countries of the WPR established a goal to eliminate measles in the region by 2012. The strategies included (1) high vaccination coverage ($\geq 95\%$) with a first and second dose of measles-containing vaccine (MCV2) through routine vaccination or catch-up and follow-up supplementary immunization activities (SIAs); and enhanced case-based epidemiological surveillance in conjunction with laboratory monitoring to identify measles virus genotype. By 2009, 21 of 37 countries and areas had $\geq 90\%$ coverage with a first dose of measles vaccine. Between 2009 and 2012, the incidence has reached a record low, with decline by 82.6% from 34.0 to 5.9 cases per million (18).

Although the countries and areas in the WPR experience an overall decrease in burden of measles, there were large numbers of cases continue in several countries. The WHO-led intensified vaccination efforts focused on Cambodia, Laos, Papua New Guinea, and Vietnam at first, yet, China and Japan, the most populous two countries accounting 80% of the region's population, were not included (19). In 2008, a total of 131,441 measles cases (98.4 per million population) were reported from China and 11,015 cases (86.1 per million population) from Japan (20). In China, although the incidence of measles decreased from 9.95 in 2008 to 0.46 in 2012, however increased in 2013 by 1.96, potentially due to immunity gaps between birth cohorts (21). In Japan, the regular vaccination schedule has been changed to two-dose schedule since 2006, however there were still estimated 5-10 thousands measles cases and 50 measles death annually (22). The outbreaks were also reported in distant countries: in Marshall Islands in 2003, Fiji in 2006, and Australia in 2006

(23). In Vietnam, although supplementary immunization activities were conducted in 2002-2003, there were outbreak of 7,948 measles cases (93 per million population) reported from 60 of 63 provinces in 2008-2010 (24).

By late 2000s, more intensified efforts by WPR countries became necessary to achieve the 2012 goal. From 1996 to 2009, 235 million children and adolescents received vaccines during a total of 94 immunization campaigns (17). By 2009, 21 of 37 WPR countries and areas had $\geq 90\%$ coverage with MCV1; 32 countries and areas provided MCV2 with 94% coverage. Since 2010, there are ongoing activities of measles supplementary vaccination with or without conjunction with oral polio vaccine campaign: 2010 in China, Federated States of Micronesia, Papua New Guinea, Tuvalu, Vietnam; 2011 in Cambodia, Laos, the Philippines; 2012 in Papua New Guinea, Solomon, Mongolia. In 2010, the largest supplemental immunization activity in history was conducted in China, with over 103 million children vaccinated (25). Although the elimination goal of measles from WPR was not achieved, elimination was achieved in 25 of 37 countries as of 2012, including Korea, Pacific Island countries, Australia, Hong Kong and Macau (26). In addition, there was resurgence of measles transmission in 2013 and 2014, particularly in China, the Philippines, Vietnam and Papua New Guinea.

In China, routine immunization of MCV1 and MCV2 were established in 1978 and 1985, respectively (27). The supplementary immunization activities were conducted in 2004, 2008, 2010, and 2011-2013, while since 2005, school entry requirement for MCV2 was implemented. The number of measles cases decreased from 5,000-25,000 between 2007-2010 to less than 3,000 in 2011-2012, however in 2014, 33,831 cases were reported by May 31 2014, which was increased by 97% compared to that during the same period in 2013. In the Philippines, supplementary immunization activities were conducted every 3-4 yr, however the coverage rate was not high and uniform enough (19). Serious major disasters from 2012 to 2013 damaged immunization service infrastructure, which may have caused an outbreak of 2,956 cases in 2013 and 10,712 cases by April 2014. In Vietnam, supplementary immunization activities were conducted in 2002-2003, 2004, 2006, 2007, 2008, 2010, and 2011-2013 targeting various age groups and regions (27). From May 2013 to 2014, measles outbreak of more than 6,000 patients occurred, potentially affected by declined MCV2 coverage due to the shortage of vaccines. The largest measles-rubella immunization campaign had launched targeting 23 million children aged 1-14 yr in 2014. In Papua New Guinea, the supplementary immunization was given every 2 yr, and covered approximately 80%-85% of coverage rate. However, the largest outbreak since 2005-2006 occurred in 2013-2014, resulting in 1,251 cases by June 2014 (27). The investigation revealed that 35% of cases between 6 months to 5 yr did not receive a MCV1 in routine immunization.

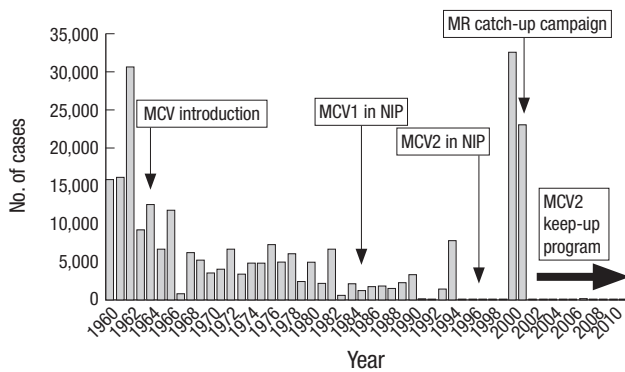


Fig. 3. Change in the incidence of measles in the Republic of Korea, 1960-2012.

EXPERIENCE IN THE REPUBLIC OF KOREA

In the Republic of Korea, the annual number of notified cases has declined after the introduction of MCV in 1965, and further down to 1,000-1,800. The MCV1 was included in the National Immunization Program (NIP) in 1985, and MCV2 became recommended by Korean Society of Pediatrics since 1997 (Fig. 3) (28). However in 2000-2001, a nationwide epidemic of measles with more than 50,000 reported cases prompted the government to implement the Five Year Measles Elimination Program that included a catch-up vaccination program targeting population with 8-16 yr of age; a keep-up program that required all children entering first grade elementary school to present a certificate of second dose of MCV vaccination (Table 2) (29).

The recommendation of MCV2 in 1997 without NIP may have posed insufficient population immunity level to prevent the 2000-2001 epidemic because of low MCV2 coverage rate (30). In 2000, the estimated MCV1 and MCV2 coverages were 86.2% and 37.7% respectively among 14,032 children selected for national survey (31). Therefore, a strong mandatory MCV2 vaccination among children such as entering elementary school became in need. The early system involved passive reporting from doctors to issue certificate of MCV2 vaccination to the parents or guardians and demonstrated adequate validity. In a survey of doctors, 59.5% of the certificates depended on the medical records of clinic, 13.5% was immunization booklets, 23.7% was re-immunizations, 1.9% was confirmation of record of other clinics, and 1.4% was parents' statements or requests without evidence (32). A randomized survey in 2010 revealed an increase of vaccination coverage of 98.3% for MCV1 and 66.1% for MCV2 (33). The recent introduction of electronic registry of all vaccination records in Korea may further improve the MCV2 coverage and validity of the coverage data (34).

The routine surveillance of measles in Korea involves a passive reporting of clinically diagnosed cases. The case-based surveillance with laboratory confirmation should be conducted in all patients with fever, measles-like rash and one of cough, co-

Table 2. Measles timeline in the Republic of Korea, 1965-2014

Timeline	Events
1965	Introduction monovalent vaccine (MCV1)
Early 1980	Introduction of MMR (12-15 months of age)
1983	Introduction of MMR into NIP
1989-1990	Outbreak of 5,809 cases
1993-1994	Outbreak of 9,386 cases
1997	Recommendation of MCV2 by Korean Society of Pediatrics (4-6 yr of age)
2000-2001	Outbreak of 52,897 cases
2001-2006	Five-Year Measles Elimination Program (1) Catch-up campaign (5.8 million) (2) Keep-up program (School entrance, 0.5-0.7 million annually) (3) Enhanced surveillance (Case-based & laboratory)
2006	Declaration of measles elimination (< 1 case/million population)
2006	Outbreak of 15 cases (Kindergarten)
2007	Outbreak of 180 cases (Nosocomial transmission)
2010	Outbreak of 93 cases (Junior high school)
2011	Outbreak of 32 cases (Gyeongnam Province)
2014	WHO verification of measles elimination : 2008-2013; 0.93 cases/million population : Average of 47.5 confirmed annual measles cases

ryza and conjunctivitis, and the collection of serum and throat swab specimens became mandatory. In 2006, the active laboratory-based surveillance was established, which involved mandatory reports from sentinel laboratories to the Korea Centers for Disease Control and Prevention (KCDC) (35). When the KCDC receives direct notification from sentinel laboratories, the investigation team immediately starts an investigation of each case. To enhance the human resource capacities of immunization, the Field Management Training Program (FMTP) was established to train annually the health workers of more than 250 public health centers located across the country.

After implementation and improvement of the program, a number of annual reported cases have declined to less than one case per million persons, and Korea became the first nation in Western Pacific to declare the elimination in 2006. Between 2002 and 2005, a decrease in measles incidence was noted, whereas cyclical increases were noted from 2006 to 2011. Most cases were in the age groups 0-23 months and 12-17 yr (36). The two unexpected outbreaks of measles that occurred during 2006 in a kindergarten in Incheon, and during 2007 in which cases that were mostly nosocomial transmission (37,38). In 2010, an outbreak occurred in a junior high school that included 74 vaccine-modified measles cases with limited symptoms that resembled measles (39).

Although Korea experienced a series of resurgence of measles due to importation and healthcare-associated transmission in infants, the overall incidence and surveillance indicators met the WHO criteria for measles elimination. Following the Third Annual Meeting of the Regional Verification Commission for Measles Elimination in the Western Pacific Region in March 2014, Korea, Australia, Mongolia, and Macau China were verified to be measles-free for the first time since the criteria for measles-

free verification were established in the region.

One of the keys to effectively control measles in Korea was the establishment of routine immunization of 2 dose before entrance to elementary school. As the population immunity reaches threshold to interrupt measles transmission among traditionally high risk group for measles infection, there are eventual shift in age from pre-school aged children to school aged children (40,41). Targeting school-aged children for school-based mass vaccination campaign therefore is a rational approach for attaining adequate population immunity and to interrupt measles transmission in high risk population. Moreover, a policy requiring measles vaccination certificate when entering schools have been successful in ensuring high vaccination coverage rate (42). The policy was also effective in decreasing measles incidence as observed in the United States, where the measles incidence was lower in states that had mandatory requirements for MCV2 at school entrance (43).

FUTURE PERSPECTIVES

As the smallpox was eradicated globally in 1980, marking the first time that humans have removed an infectious disease, this triumph should be replicated in the case of measles and other vaccine-preventable diseases. Yet, evaluation of the ongoing resurgence of measles in the Korea has been helpful in understanding the reasons for continued disease occurrence in the countries and areas of WPR. Reports from most outbreaks were caused by non-vaccinated or under-vaccinated population, importation, and weak surveillance system. The continued occurrence of measles demonstrates that the virus continues to circulate around the globe, albeit at low levels of incidence in the Regions of America and Korea. The recent adoption of two-dose vaccination strategy by China and Japan may contribute to the dramatic reduction of measles cases in the WPR. Because not all countries in the WPR have solid health infrastructure and system, continuous supplementary vaccination activities including keep-up, follow-up, and mop-up strategies would be necessary. Full investigation of remaining measles cases, including confirmation of genotypes and documentation of epidemiological assessment, would provide additional opportunities for prevention. At present, most cases of measles in the WPR occur in preschool-aged children and in unvaccinated or partially vaccinated children aged 1-2 yr old. These observations reinforce the need to ensure universal and timely vaccination against measles in the WPR, and sharing the experiences from Korea would be helpful to other member states and areas.

DISCLOSURE

No potential conflicts of interest are declared.

AUTHOR CONTRIBUTION

Study design: Lee JK. Writing: Choe YJ. Revision of the manuscript: all authors. Supervision and interpretation of data: Jee Y, Oh MD. Approval of final manuscript: all authors.

ORCID

Young June Choe <http://orcid.org/0000-0003-2733-0715>

Youngmee Jee <http://orcid.org/0000-0001-5369-6628>

Myoung-don Oh <http://orcid.org/0000-0002-2344-7695>

Jong-Koo Lee <http://orcid.org/0000-0003-4833-1178>

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