

Short Communication

Detection of Measles Virus Genotypes B3, D4, D5, D8, and H1 in the Surveillance System in Hokkaido, Japan, 2006-2015, the Last Decade toward the Elimination

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SUMMARY: Measles is an acute and highly contagious disease caused by measles virus (MeV). The government of Japan, following the last epidemic in 2007 and 2008, which was caused by genotype D5 strains, introduced a catch-up-vaccination program for teenagers during Japan fiscal years 2008–2012 and a mandatory case-based reporting system for the nationwide elimination. Furthermore, laboratory confirmation of measles cases by genotyping of isolates has been performed to clarify the source of infection and support the interruption of measles cases. Owing to these preventive measures, the number of measles cases has been steadily decreasing after the last epidemic. In March 2015, Japan was internationally verified as having achieved measles elimination by the World Health Organization Regional Office for the Western Pacific. The continuous elimination of measles and high levels of vaccination coverage for MeV have been maintained nationally. However, imported or import-associated cases of measles have sporadically occurred during this time. After the last nationwide epidemic, 17 imported or import-associated measles cases (MeV strains identified as genotypes H1, D4, D8, and B3) were reported in Hokkaido, the northern islands of Japan. In this study, we present the occurrence of measles and surveillance activities in Hokkaido during 2006–2015.

Measles, caused by measles virus (MeV), is an acute and highly contagious disease, characterized mainly by high fever and cough followed by the appearance of a systemic maculopapular rash (1). Worldwide, measles is one of the most infectious diseases with high mortality, especially in many developing countries. However, introduction of an effective vaccination program for measles that maintains a high level of population immunity can lead to elimination of this infectious diseases (2). Although MeV is serologically monotypic, its genetic phylogeny of wild-type strains is presently divided into 8 clades (A to H) and subdivided into 24 genotypes (3). Genetic characterization of MeV is useful in the identification of the origin of isolates, because each genotype is distributed chronologically and geographically. To predict the transmission route and the epidemiological background of MeV, the World Health Organization (WHO) recommends the sequencing of the 450 nucleotide region encoding the C-terminal 150 amino acids of the nucleoprotein (4).

Since 2006 in Japan, a revised measles-rubella vacci-

nation program has been routinely implemented; children receive 2 doses of the vaccine, the first dose at 1 year of age and second at 5–6 years. However, a nationwide measles epidemic occurred in Japan in 2007 and 2008, mainly among teenagers (5). This epidemic led the Japanese Government to achieve high vaccination coverage, and to introduce a nationwide supplemental immunization activity for 13 and 18 years old age groups during Japan fiscal years 2008–2012 (5). In addition, beginning in January 2008, the surveillance system for measles was changed from a sentinel surveillance system to a mandatory case-based reporting system. Eventually, the number of reported measles cases in Japan decreased dramatically from 11,013 in 2008 to 35 in 2015 (6). In particular, genotype D5 identified in the epidemic during 2006–2008, has not been detected since May 2010 in Japan. More recently, all MeV isolates in Japan, genotypes H1, D9, D8, D4, G3, and B3 are considered to be imported or import-associated strains (7). With this situation, Japan was verified as having achieved the measles elimination by the WHO Regional Office for the Western Pacific in March 2015 (8). In this study, we report on the recent epidemiologic status of measles in Hokkaido to contribute to the continuous elimination of measles in Japan.

Clinical specimens of throat swab, blood, and urine were collected from patients suspected of having measles chiefly by the clinical symptoms such as fever, cough, rash, and/or the presence of the Koplik-like spots. These specimens were submitted to the Prefec-

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tural or Municipal Public Health Institutes to confirm each causative agent. According to the method described previously, laboratory testing was performed by the presence of immunoglobulin M antibodies or detection of the viral genomes, or both (9).

These investigations were performed following approval by the Ethics Committee of Hokkaido Institute of Public Health.

The incidence of measles in Hokkaido during 2006–2015 is summarized in Table 1. During this period in Hokkaido, MeV genotypes D5, H1, D4, D8, and B3 were detected. In 2007 and 2008, due to an occurrence of a national outbreak of measles involving genotype D5 strains, a total of 850 and 1,462 cases were identified in Hokkaido, respectively (10,11). Subsequently, a dramatic decrease of measles cases was observed in 2009; 17 cases of measles were reported to the case-based reporting system, however, laboratory confirmation of MeV was not performed in every case, partly because of the lack of specimens. In 2010, the reported number of measles cases declined to 5, and 2 of these were confirmed as imported cases based on genotyping. One imported case was a visitor from China, and the other was a Japanese returnee from India; genotypes H1 and D4 were identified, respectively (11). In 2011, 8 cases were reported (9). Among these, genotype D8 was identified in 2 cases. While they had no history of travel to foreign countries, both had visited the same regional hospital almost simultaneously. Although the source of the virus was not clarified, the occurrence of nosocomial viral transmission was strongly suggested in these cases.

In 2014, a regional measles endemic caused by the genotype B3 had occurred (12). The initial case had a history of travel to the Philippines for 3–18 days before the onset of rash. Within 2 months, a total of 12 measles cases were reported in cities located within a 50-km radius. Genotyping in these cases showed identical measles types, although 1 case was not tested. Therefore, this endemic was deemed an import-associated outbreak. Additionally, imported measles cases caused by genotype D8 strains were further reported in 2014 from

Indonesia and 2015 from Malaysia. Thereafter, no more cases of measles were reported in Hokkaido until May 2016. Besides, one and 2 measles cases were reported in 2012 and 2013, respectively. However, the genome of MeV was not detected from these patients, therefore, it was unknown whether they were definite measles cases.

Owing to activities related to maintaining the achievement of measles elimination in Japan, no indigenous cases of measles have been reported in recent years in Japan (6). However, the occurrence of imported or import-associated cases has been reported sporadically. Even though the immunization coverage levels were high among residents, measles caused by imported MeV is likely imperative because of the continuous viral transmission that still occurs in many regions globally (6,13). Additionally, unvaccinated individuals and individuals who refuse vaccination generally increase the risk of transmission of MeV (14). Except for individuals who are not recommended to be vaccinated for medical indications, everyone should receive at least 2 doses of a measles-containing vaccine. Furthermore, prior to going abroad, susceptible individuals should be vaccinated (6).

Nosocomial transmission was probably the source of measles transmission in some of the cases in this study (12). Prevention of this type of transmission is an urgent problem. In one of these cases, despite suffering from the symptoms of measles, it was not initially suspected and diagnosed correctly. This index patient had visited 1 hospital and 2 clinics and continuously spread the virus to some susceptible persons. Now, physicians increasingly have little experience in diagnosing a case of measles, because nationwide elimination has been achieved. To avoid misdiagnosis, physicians must always consider the contagious diseases in cases with suspicious symptoms. It is also important that medical practitioners who lack immunity or have weakened immunity to measles are vaccinated. In addition, when a new case of measles is notified, the sharing of accurate epidemiologic information is highly critical in performing preventive measures, which will result in maintaining the elimination status successively.

Table 1. Summary of measles cases in Hokkaido, Japan, 2006–2015

| Yr | Japan | | Hokkaido | | | | |
|--------------------|----------|----------|--|----------|------------------------|-----------------------------|------|
| | Case No. | Case No. | Case No. confirmed with laboratory testing (%) | Genotype | Pattern of occurrence | Traveling destination | Ref. |
| 2006 ¹⁾ | 555 | 3 | – | – | – | – | 10 |
| 2007 ¹⁾ | 4,101 | 850 | – | D5 | Endemic | – | 10 |
| 2008 | 11,013 | 1,462 | 408 (27.9) | D5 | Endemic | – | 11 |
| 2009 | 732 | 17 | 11 (64.7) | – | Endemic | – | 11 |
| 2010 | 447 | 5 | 4 (80) | H1, D4 | Sporadic | China ²⁾ , India | 11 |
| 2011 | 439 | 8 | 8 (100) | D8 | Sporadic / Transmitted | – | 9 |
| 2012 | 283 | 1 | 1 (100) | – | Sporadic | – | 9 |
| 2013 | 229 | 2 | 2 (100) | – | Sporadic | – | – |
| 2014 | 462 | 13 | 13 (100) | B3, D8 | Sporadic / Transmitted | Philippines, Indonesia | 12 |
| 2015 | 35 | 1 | 1 (100) | D8 | Sporadic | Malaysia | – |

¹⁾: Case numbers in 2006 and 2007 were based on those reported under 2 not-mandatory sentinel (pediatric and adult) surveillance systems (5).

²⁾: A visitor from China.

The increased international travel has led to larger numbers of visitors from other countries, especially Asian countries to Hokkaido recently (15). These countries include, for instance, China, Malaysia, and Mongolia, where many cases of measles still occur (13). To achieve the eradication of measles, with attention to the measles incidence not only in Asia but also in the world, an adequate vaccination program for susceptible individuals, active measles surveillance, vigilance by medical staff and practitioners, and performance of the laboratory confirmation tests should be continued.

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Conflict of interest None to declare.

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