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Risk Assessment for Measles – Japan, March 2024

February 22, 2024 National Institute of Infectious Diseases Research and Professional Development

Center for Field Epidemic Intelligence, Research and Professional Development Center for Surveillance, Immunization, and Epidemiologic Research

Center for Emergency Preparedness and Response

■ Background

The World Health Organization (WHO) defines "measles elimination" as the absence of sustained transmission of the measles virus, whether of domestic or international origin, for at least 12 months in a country or region with a well-performing surveillance system¹⁾.

Japan was certified by the WHO as having achieved measles elimination status in 2015. Efforts have been made to maintain this status in accordance with the "Guidelines for the Prevention of Specific Infectious Diseases Related to Measles" ²⁾, with the aim of preventing occurrences and outbreaks.

Despite achieving measles elimination, there have been multiple outbreaks triggered by travelers from overseas, outbreaks in healthcare settings, and outbreaks in populations with low measles vaccination coverage. The annual reported cases reached a peak of 744 in 2019, the highest since achieving elimination status.

In the following year, 2020, the annual reported cases decreased dramatically to 10 due to travel restrictions and other factors attributable to the COVID-19 pandemic. Furthermore, in each of 2021 and 2022, the number decreased to 6 cases. In 2023, however, when COVID-19 border measures were relaxed⁶, the annual number of notifications increased to 28 cases (Figure 1).

Given that recent measles cases, including those predating the COVID-19 pandemic, were triggered by imported cases^{7,8)}, the risk of measles importation from overseas is expected to increase further in the future.

Against this backdrop, a risk assessment was conducted regarding the potential occurrence and spread of measles cases domestically, taking into account the results of the Infectious Agents Surveillance Report, National Epidemiological Surveillance of Infectious Diseases and National

Epidemiological Surveillance of Vaccine-Preventable Diseases, and the recent situation of overseas occurrence.

■ Domestic situation in 2023, as of January 5, 2024

During the period from the 1st to 52nd epidemiological week of 2023, a total of 28 measles cases were reported, with reports confirmed in each of the 19th to 27th week (Figure 1). Cases were reported from various locations nationwide, including Hokkaido, Akita, Ibaraki, Chiba, Tokyo, Kanagawa, Shizuoka, Aichi, Osaka, Hyogo, and Tottori. Following importation into Japan, an event involving transmission during domestic transportation was reported^{9,10}.

Cases were reported from different residences, workplaces, and locations of activity, requiring multiple municipalities with independent jurisdiction to collaborate with each other to ensure prompt information-sharing¹¹⁾.

By sex and age group, males accounted for 68% (19 cases), with a median age of 31 years (interquartile range: 1-61 years). In particular, the age group of 20-39 years was predominant, accounting for more than half (64%, 18 cases) of all reported cases.

The vaccination history for measles-containing vaccine* in reported cases was as follows: 6 had no history of vaccination, 11 had received one dose, 4 had received two doses, and 7 had unknown vaccination status. The proportion of individuals who had not completed two doses of vaccination, including those with unknown status, accounted for 86% (24 cases). In the 20-39-year age group, 28% (5 cases) had never been vaccinated (Figure 2).

Typical measles ("measles") accounted for 82% (23 cases) and modified measles accounted for 18% (5 cases), both based on mandatory diagnostic testing for reporting. Several cases had a history of visiting multiple medical facilities before diagnosis ^{12,13}).

Regarding the estimated place of infection, "overseas" accounted for 21% (6 cases), with travel destinations including Indonesia and India. Reports from places within Japan accounted for 68% (19 cases), while reports with uncertain origin, either domestic or international, accounted for 11% (3 cases).

Among the cases with identified genotypes, genotype D8 was found in 15 cases, and undetermined in 2 cases. Currently, genotypes D8 and B3 are detected worldwide, with D8 being particularly prevalent in Southeast Asia, the Western Pacific, and Europe¹⁴).

As of February 14, there have been no reported cases in 2024¹⁵).

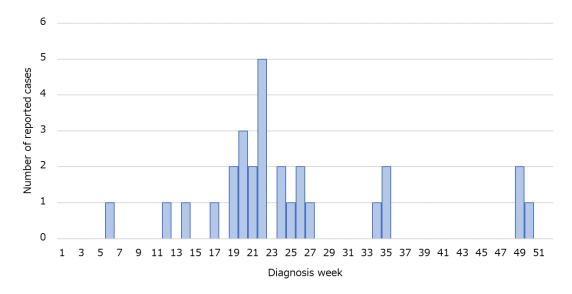


Figure 1. Incidence of Measles in Japan (n=28, weeks 1-52 of 2023, as of January 5, 2024)

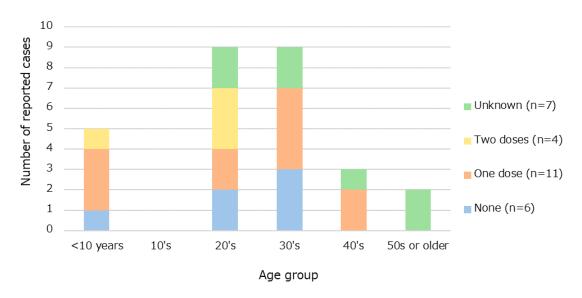


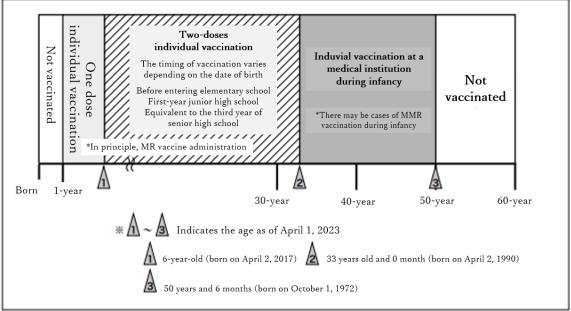
Figure 2. Number of Measles Reports by Age Group and Measles-Containing-Vaccine History* (n=28, weeks 1-52 of 2023, as of January 5, 2024)

* Based on registration information from the National Epidemiological Surveillance of Infectious Diseases System

■ Vaccination coverage and antibody positivity of measles in Japan

Measles vaccination has started as a voluntary vaccination since 1966 and was introduced as a routine vaccination in October 1978. At that time, the target age for routine vaccination was from 12 months to less than 72 months old. In fiscal year 1995, this was changed to be from 12 months to less than 90 months old. In fiscal year 2006, the combined measles and rubella (MR) vaccine given in two doses

was introduced, and the target age for the first dose is from 12 months to less than 24 months, and that for the second dose is from 5 years to less than 7 years among children in the year before elementary school enrollment. Subsequently, with the goal of eliminating measles domestically, from 2008 to 2012, opportunities for the second dose of the MR vaccine were provided. This was aimed at closing the immunity gap among teenagers, the age group involved in many of the previous outbreaks. The target age ranged from first-year junior high school students to third-year high school students. The routine vaccination status by age group implemented to date is in Figure 3.



The 4th Health Sciences Council Preventive Vaccination and Vaccine Subcommittee Preventive Vaccination

Figure 3. Routine vaccination status for measles-containing vaccines, which started in October 1978.

Reproduced from the "2023 Q&A Collection on Vaccination" by the Japan Association of Vaccine Industries, 2023 (http://www.wakutin.or.jp/medical/)

Japan aims to achieve and maintain vaccination coverage of at least 95% for two routine doses of the MR vaccine to maintain measles elimination status. The nationwide MR vaccine coverage for fiscal year 2022 was 95.4% for the first dose and 92.4% for the second dose. The first dose coverage showed an increase from 93.5% in the previous year, but the second dose coverage showed a decrease from 93.8%, falling below 90% in three prefectures.

The status of measles antibody titer by age/age group in fiscal year 2022 is shown in Figure 4. The proportion of individuals with a positive measles antibody titer of 1:16 or higher, which is considered indicative of measles antibody positivity in person aged 2 years or older, was maintained at 95% or higher in almost all age groups, with an overall rate of 96.2%. However, the proportion of individuals with antibody titers of at least 1:128, which is the level considered necessary to prevent the onset of

measles or modified measles, was 85.7% overall. In certain age groups, especially teenagers, the coverage did not exceed 90%.

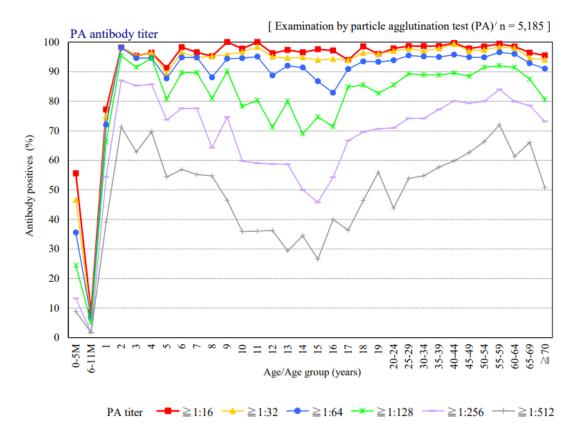


Figure 4. Age distribution of measles particle agglutination antibody positivity in Japan, 2022, reproduced from the National Epidemiological Surveillance of Vaccine-Preventable Diseases, 2022 (https://www.niid.go.jp/niid/ja/y-graphs/1600-yosoku-index-e.html)

■ Global measles situation

In 2020 and 2021, the number of reported measles cases worldwide was 93,840 and 59,619, respectively. This was a sharp decrease from 2019, when there were 541,401 cases, with the numbers falling by more than 80%. However, there has been increase since 2022, and as of February 2024, the number of reported cases in the year 2023 has reached 306,291¹⁴ (Figure 5). The decline in reported cases in 2020 and 2021 is thought to have been influenced by improved immunity following the 2017-2019 measles outbreak, as well as the negative impact on health-seeking behaviors and testing infrastructure during the COVID-19 pandemic^{17,18}).

In 2023, the WHO's regions reporting the majority of measles cases were the Southeast Asia Region (SERO), the Eastern Mediterranean Region (EMR), and the African Region (AFR), collectively accounting for 79% of all cases. The number of reported measles cases from the European Region (EUR) increased more than 30-fold compared with the previous year, with severe cases requiring

hospitalization and deaths also reported. This resurgence of measles is largely attributed to regression in vaccination coverage in the countries of those regions between 2020 and 2022¹⁹⁾. In particular, Kazakhstan has recorded the highest number of cases, with 13,677 in 2023 (3,269 cases in 2022, 2 cases in 2021, 4 cases in 2022). Among the reported measles cases in Kazakhstan, 65% were children under 5 years of age who missed routine immunization doses during the COVID-19 pandemic²⁰⁾.

There has also been an increase in measles cases across the UK since October 2023, reaching a total of 368 cases annually. This represents the highest number of reported cases since the beginning of the COVID-19 pandemic in the country. Among the reported cases, 63% involved children under the age of 10 years and 19% of the cases involved teenagers or young adults aged 15-34 years. As of January 30, there have already been 127 reported cases in 2024, indicating an increasing trend in case reporting^{21,22)}. Regionally in the UK, there was a high number of reports from the West Midlands, with 216 cases reported since October 2023 (as of January 18, 2024). Approximately 80% of these cases were reported from Birmingham^{23,24)}.

The US has achieved and maintained measles elimination status since 2000. Since December 2023, an increase in imported measles cases has been reported. Among the reported 26 cases (17 cases in December 2023, 9 cases in January 2024), 7 imported cases from overseas were identified, leading to two outbreaks involving more than 5 cases each. The Centers for Disease Control and Prevention (CDC) issued an alert for healthcare providers on January 25, urging caution due to the occurrence of imported cases associated with the global increase in measles patients and outbreaks among susceptible populations initiated by imported cases²⁵.

To achieve sufficient herd immunity against measles, coverage of at least 95% with two-dose measles-containing vaccines must be achieved and maintained. However, at the global level, the first-dose measles-containing vaccine (MCV1) coverage was 81% in 2021 and 83% in 2022. These were the lowest levels of MCV1 recorded since 2009. Additionally, the coverage for the second dose of measles-containing vaccine (MCV2) reached 74%²⁶⁾ in 2022, the highest level since 2000. However, this was far from the target coverage of at least 95%. Now, there is naturally growing concern about a further increase in measles cases due to the accumulated number of susceptible individuals.

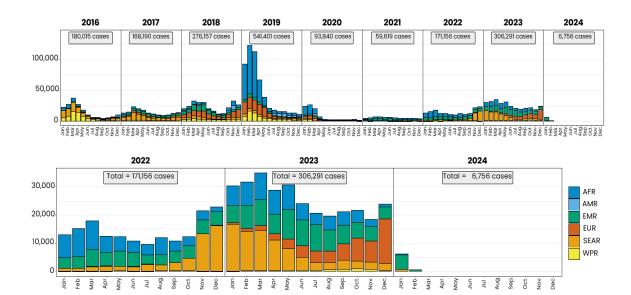


Figure 5. Distributions of measles cases by month and WHO region (2016-2024, as of February 2024)

Reproduced from https://www.who.int/teams/immunization-vaccines-and-biologicals/immunization-analysis-and-insights/surveillance/monitoring/provisional-monthly-measles-and-rubella-data

Risk assessment

- (1) Current situation and challenges
- The number of domestically reported measles cases, which had decreased in 2021 and 2022 due
 to the COVID-19 pandemic, increased substantially in 2023, with cases believed to be triggered
 by imported cases from overseas.
- In 2023, reported measles cases have been increasing globally since the COVID-19 pandemic subsided. The risk of importation of measles virus from overseas into the country has risen due to increased international travel, which had been restricted during the COVID-19 pandemic. Southeast Asia in particular is one of the areas globally with a high number of reported measles cases, and it is also a region with a large number of visitors to and from Japan²⁷⁾.
- In Japan, based on the routine vaccination schedule, individuals born on or after April 2, 1990, have had the opportunity to have two routine doses with measles-containing-vaccine. However, considering the age groups of measles cases reported domestically, it is evident that even within this cohort, infections are occurring in individuals who have not completed the two doses of vaccination.
- Measles antibody positives in Japan has been maintained at 95% or higher across most age groups.
 However, the nationwide measles-containing-vaccine coverage for fiscal year 2022 was slightly lower than that before the COVID-19 pandemic.

The decline in measles-containing vaccine coverage may result in an increase in the number of

individuals susceptible to measles virus infection in Japan. This raises concerns about potential outbreaks of measles, including severe cases, imported by returnees or travelers from overseas.

(2) Countermeasure

- There are countries and regions where the incidence of measles is persistent or has recently increased rapidly. For travel to countries or regions where there has been an increase in cases, it is recommended that travelers confirm their history of two doses of measles-containing vaccine before departure. Two doses of vaccination can prevent infection in travelers and prevent the further spread of virus upon their return.
- For those who have frequent contact with returnees or travelers from overseas, it is recommended
 that they confirm their vaccination history of two doses of measles-containing vaccine in order to
 prepare for the risk of importation from overseas.
- For individuals at high risk of exposure to measles patients, such as healthcare workers, it is
 important that they verify their vaccination history of two doses of measles-containing vaccine as
 a precaution, even during periods with no measles outbreaks.
- To prevent from the spread of infection domestically, it is essential to promptly report all suspected measles cases, conduct appropriate diagnostic testing, rapidly investigate and response contacts, and conduct proactive sensitization campaigns for the public through administrative agencies, medical institutions, and medical associations. In addition, where there is a risk of widespread transmission, it important to share information rapidly among relevant authorities including local and national government.
- Due to the decline in routine vaccination coverage, there is a growing number of susceptible individuals who do not have sufficient antibody immunity. Thus, there is the potential for domestic transmission when measles virus is introduced. To prevent the spread of infection, it is necessary to maintain routine vaccination coverage of at least 95% and to sustain a high level of antibody immunity against measles.
- Some cohorts have received only one dose of routine vaccination, and there are also individuals who have not completed the recommended two doses despite being eligible. Therefore, it is important to consider vaccination for people who have an uncertain history of two doses of measles-containing vaccine, based on records such as the Maternal and Child Health Handbook.

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