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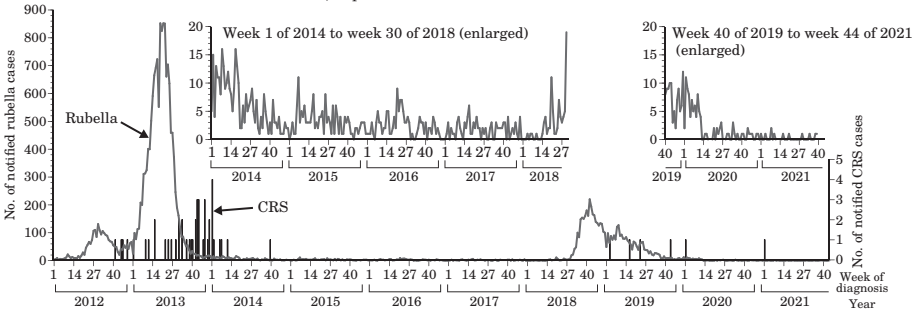
National Institute of Infectious Diseases and
Tuberculosis and Infectious Diseases
Control Division,
Ministry of Health, Labour and Welfare

<THE TOPIC OF THIS MONTH>
Rubella and congenital rubella syndrome in Japan as at November 2021

Figure 1. Weekly number of notified rubella cases and congenital rubella syndrome (CRS) cases, week 1 of 2012 to week 44 of 2021, Japan



(National Epidemiological Surveillance of Infectious Diseases: as at 20 December 2021)

Rubella is an acute infectious disease caused by the rubella virus and is characterized by fever, rash, and lymphadenopathy. Pregnant women who are insufficiently immunized against rubella and infected with the rubella virus may experience stillbirth, miscarriage, or the birth of an infant with congenital rubella syndrome (CRS), which manifests as various symptoms including cardiac disease, deafness, and cataracts. The risk of CRS is especially high in maternal infections through 20 weeks of pregnancy. There is no specific treatment for rubella or CRS, but it is preventable with the administration of rubella-containing vaccine.

In 2014, the Ministry of Health, Labour and Welfare (MHLW) developed the "Guidelines for the Prevention of Specific Infectious Diseases Related to Rubella" (hereinafter referred to as the "Guidelines"), which set the direction of policies aimed at the elimination of CRS occurrence as early as possible and the achievement of rubella elimination by fiscal year (FY) 2020. In addition, in response to the large-scale outbreak of rubella, mainly among adult males in 2018-2019, MHLW compiled the "Framework for Additional Measures Concerning Rubella" on December 13, 2018, and decided to implement routine immunization (5th "round" of routine vaccination against rubella) for men born between April 2, 1962 and April 1, 1979, who had no opportunity to receive routine vaccination against rubella and have a lower seroprevalence of rubella-specific antibody compared to other age groups; this routine vaccination activity was to operate for approximately three years, based on the premise of antibody testing.

During 2020-2021, the COVID-19 pandemic had a large impact on rubella control measures both in Japan and abroad, including a decline in immunization coverage.

Surveillance of Rubella and CRS under the National Epidemiological Surveillance of Infectious Diseases (NESID)

Rubella is a notifiable, Category V infectious disease under the Infectious Diseases Control Law (https://id-info.jihs.go.jp/niid/images/iasr/36/425/de4251.pdf). In recent years, outbreaks occurred nationally in 2012-2013 and 2018-2019, with a high number of case patient reports (Fig. 1). Currently, the number of case patient notifications has decreased to 101 cases in 2020 and 11 cases as at week 44, 2021. In 2018-2019, approximately 95% of rubella case patients were 20 years or older, and male case patients were approximately 3.9 times more frequent than female case patients, indicating a predominance of adult males (Fig. 2 on p.2). The age groups with the highest number of case patient notifications in 2018-2019 were 40-44 years for men and 25-29 years for women. This trend in case patient distribution was also observed in 2020 but was less apparent in 2021 when case patient notifications declined dramatically. Among rubella case patients in the 2018-2019 epidemic, the percentage of those with a history of vaccination was low (6-8% for "one dose" and 1-2% for "two or more doses") (Fig. 3 on p.2).

CRS is also classified as a Category V infectious disease requiring the notification of all cases based on the Infectious Diseases Control Law (https://id-info.jihs.go.jp/niid/images/iasr/36/425/de4252.pdf), and 45 cases of CRS were notified from 2012 to 2014 in association with the rubella epidemic (Fig. 1). Thereafter, there were no notifications from 2015 to 2018, but four cases were notified in 2019, one in 2020, and one in 2021. The recorded history of rubella-containing vaccine receipt in the mothers of the six CRS case patients notified in 2019-2021 was three with one-dose vaccination, three unknown, and none with two-dose vaccination (see p.3 of this issue).

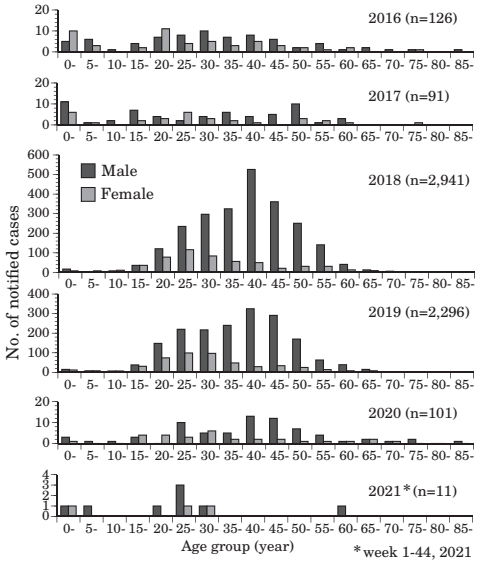
Status of laboratory testing for rubella

To strengthen rubella surveillance, the Guidelines were partially revised in 2017; as a rule, testing is required from 2018. During 2014-2017, only 60-75% of rubella case notifications were confirmed by testing, while in 2018-2020, after the revision of the Guidelines, more than 90% of cases were based on laboratory confirmation (Fig. 4 on p.2). Public Health Institutes are continuously monitoring the situation by detecting rubella virus genes and analyzing the viral genomes using quality-controlled methods (see p.4 of this issue). A study by a Public Health Institute showed that the time from the onset of fever to the onset of rash in rubella case patients is often –1 to 2 days, and this information is useful for screening cases for which rubella testing should be performed

(Continued on page 2′)

(THE TOPIC OF THIS MONTH-Continued)

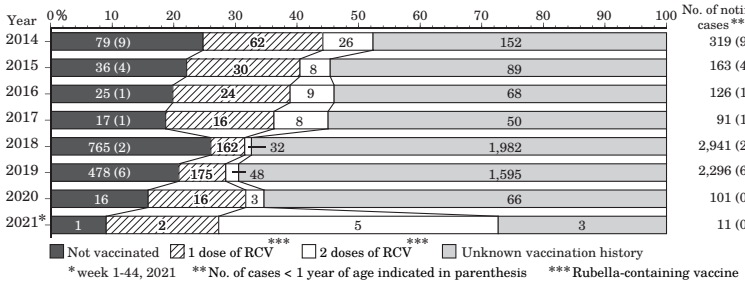
Figure 2. Age distribution of notified rubella cases by age group and gender, 2016-2021*, Japan



(National Epidemiological Surveillance of Infectious Diseases: as at 20 December 2021)

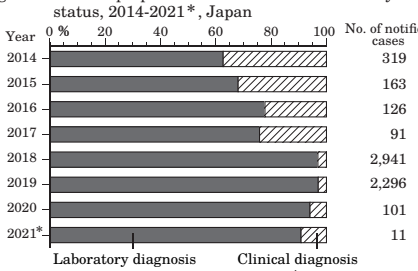
Figure 3. No. and proportion of notified rubella cases by vaccination status, 2014-2021*, Japan

(National Epidemiological Surveillance of Infectious Diseases: as at 20 December 2021)



*week 1-44, 2021 **No. of cases < 1 year of age indicated in parenthesis ***Rubella-containing vaccine

Figure 4. No. and proportion of notified rubella cases by diagnosis status, 2014-2021*, Japan



(National Epidemiological Surveillance of Infectious Diseases: as at 20 December 2021)

as a priority (see p.6 of this issue). A case in a pregnant woman who tested positive for IgM antibody against rubella but was consistently negative for both hemagglutination-inhibiting (HI) antibody and IgG antibody against rubella has been reported; careful interpretation of test results is necessary because of the presence of false positive IgM test results (see p.7 of this issue).

National Epidemiological Surveillance of Vaccine-Preventable Diseases (NESVPD) and survey on vaccination coverage of rubella-containing vaccines

To evaluate the above-mentioned additional measures, the NESVPD survey on rubella susceptibility in FY2020 had planned to increase the number of male subjects aged 40-59 years, including those eligible for the 5th round of routine immunization, in addition to those surveyed in previous years. However, due to the impact of the COVID-19 epidemic, the number of survey subjects was greatly reduced compared to previous years, with 3,164 subjects (1,783 males and 1,381 females) from 14 prefectures (Fig. 5 on p.3). The prevalence of rubella HI antibody titers of 1:8 or higher was generally 90% or more in each of the age groups among those 2 years of age through those in their early 30s, for both males and females (see p.9 of this issue). In women, almost all age groups among those in their late 30s to 50s had a seroprevalence of 90% or more, while the seroprevalence for men in their 40s to 50s was lower at approximately 80%. The seroprevalence among males born between FY1962 and 1978, who are eligible for the 5th round of routine immunization, has not changed substantially in the last decade, and the effect of the 5th round of routine immunization has not been seen at the time of the present survey.

Since FY2006, routine immunization has been administered to one-year-old children (first dose) and children in the year before entering elementary school (second dose), and since FY2008, a nationwide survey on the coverage of rubella-containing vaccine receipt has been conducted annually in cooperation with prefectural and municipal governments (see p.11 of this issue). Due to the impact of the COVID-19 pandemic, the immunization coverage of the first dose decreased to 95.4% in FY2019, but recovered to 98.5% in FY2020. The immunization coverage for the second dose in FY2020 was 94.7%, which did not achieve the target of 95% or more. Among those eligible for the 5th round of routine immunization, 23.5% had been tested for rubella antibodies through September 2021 and 4.9% of the eligible men had received a subsequent vaccine (https://www.niid.go.jp/niid/images/epi/rubella/2021/rubella211104.pdf).

Challenges for the future

As a result of strengthening rubella control measures, including vaccination and surveillance globally, rubella elimination has been verified in 83 countries by October 2021 (see p.12 of this issue). On the other hand, the heterogeneity of population immunity at the national and subnational levels, the accumulation of susceptible populations among older children and adults, lack of resources to implement plans, and incomplete surveillance remain as challenges. The number of rubella cases reported in the Western Pacific Region of the World Health Organization (WHO) in 2020, the year of the COVID-19 pandemic, decreased substantially from the previous year; however, a decline in immunization coverage has been reported worldwide, which is of concern as a cause of producing a new group of susceptible individuals. Given these new challenges, the WHO adopted the “Measles and rubella strategic framework: 2021-2030”.

In Japan, many adult males remain susceptible, and additional measures are currently being implemented to counteract this problem. However, it is anticipated that it will be difficult to achieve the goals for antibody testing and vaccination coverage by the end of the period in March 2022, and revision of the project is under discussion (45th Health Science Council, Subcommittee on Immunization and Vaccine, Subcommittee on Basic Immunization Policy, 55th Health Science Council, Subcommittee on Infectious Diseases). To overcome the current situation in which the vaccination coverage in adult males eligible for the 5th round of routine rubella vaccination is not increasing as expected, the “Rubella Zero” Project is promoting educational activities regarding rubella in cooperation with associated academic societies and organizations (see p.13 of this issue). Although the number of reported rubella cases in Japan is currently low, there is a concern that rubella could be brought in from overseas and re-circulate in Japan after the movement restrictions introduced to control the COVID-19 pandemic are lifted. It is important to continue to maintain and strengthen rubella control measures, including vaccination and surveillance activities, to prevent domestic circulation and to achieve the elimination of rubella in Japan.

The statistics in this report are based on 1) the data concerning patients and laboratory findings obtained by the National Epidemiological Surveillance of Infectious Diseases undertaken in compliance with the Act on the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases, and 2) other data covering various aspects of infectious diseases. The prefectural and municipal health centers and public health institutes (PHIs), the Department of Environmental Health and Food Safety, the Ministry of Health, Labour and Welfare, and quarantine stations, have provided the above data.

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