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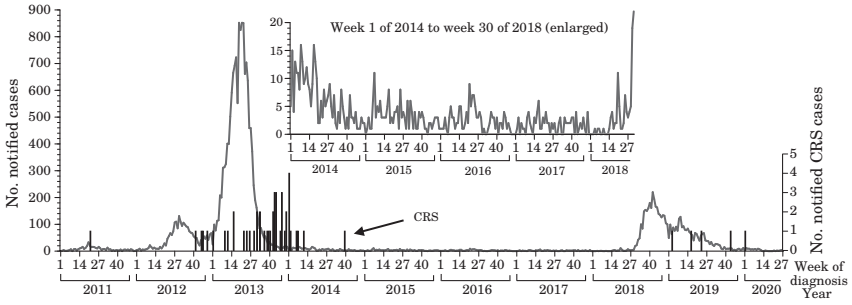
National Institute of Infectious Diseases and
Tuberculosis and Infectious Diseases
Control Division,
Ministry of Health, Labour and Welfare

<THE TOPIC OF THIS MONTH>
Rubella and congenital rubella syndrome in Japan as at July 2020

Figure 1. Weekly number of notified rubella cases and congenital rubella syndrome (CRS) cases, week 1 of 2011 to week 27 of 2020, Japan



(National Epidemiological Surveillance of Infectious Diseases: as at 7 July 2020)

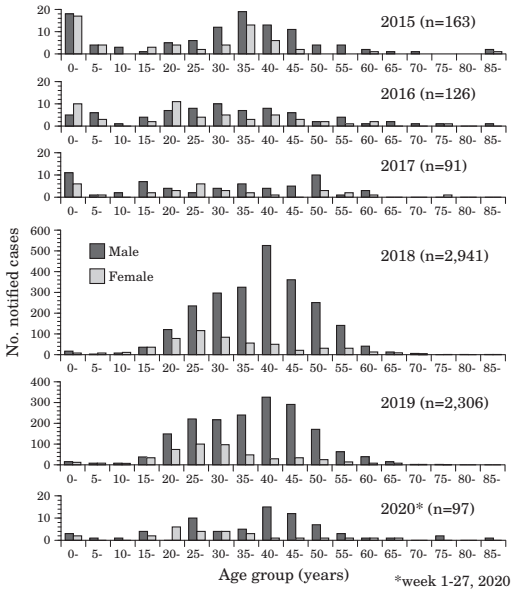
Rubella is an acute infectious disease caused by the rubella virus, and is characterized by fever, rash, and lymphadenopathy. Rubella virus infection in pregnant women, especially up to 20 weeks of gestation, may result in prenatal transmission to the fetus and congenital rubella syndrome (CRS), which presents as various manifestations including heart defect, hearing loss, and cataract. Although there are no specific treatments for rubella or CRS, they can be prevented by rubella-containing vaccines.

In response to the large-scale outbreak of rubella, mainly among adult males, since July 2018, the Ministry of Health, Labour and Welfare (MHLW) compiled the "Additional Measures on Rubella" (hereinafter referred to as "Additional Measures") in December 2018. MHLW decided to conduct routine vaccinations against rubella for males 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 than other age groups; this routine vaccination activity was to operate for approximately three years, with the condition that the vaccinee first receive an antibody test (5th "round" of routine vaccination against rubella) (see p.155 of this issue).

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

Rubella is classified as a Category V Infectious Disease requiring notification of all cases (https://www.niid.go.jp/niid/images/iasr/36/425/de4251.pdf). After the nationwide rubella epidemic of 2012-2013, the number of reported cases remained low during 2014-2017, but in 2018-2019, the epidemic recurred, mainly in metropolitan areas, with 2,941 cases reported in 2018 and 2,306 cases reported in 2019 (as of July 7, 2020) (Fig. 1). Outbreaks were reported in workplaces, clubs in entertainment districts (see p.156 of this issue), and Japanese language educational institutions (see p.157 of this issue). The number of reported cases decreased in 2020, with 97 cases reported through week 27. In 2018-2019, approximately 95% of all reported cases were in adults and approximately 80% were in males (Fig. 2). The age groups with the highest number of case reports in 2018-2019 were 40-44 years for males and 25-29 years for females. Assessment of the immunization history of rubella patients in the epidemic years of 2013 and 2018-2019 indicated that the percentage of patients with "no history of vaccination" and "unknown history of vaccination" was high (21-30% and 64-69%, respectively), whereas that of those with "one dose of vaccination" and "two or more doses of vaccination" was low (5-8% and 1-2%, respectively). This suggests that outbreaks are mainly occurring among people who have never been vaccinated (Fig. 3). Rubella vaccination is effective for acquiring immunity

Figure 2. Age distribution of rubella cases by sex, 2015-2020*, Japan



(National Epidemiological Surveillance of Infectious Diseases: as at 7 July 2020)

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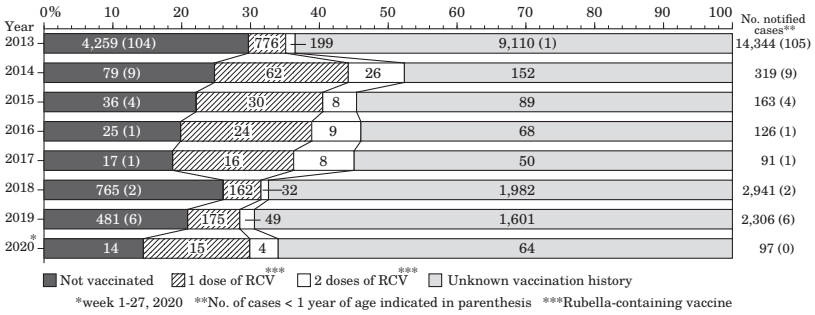
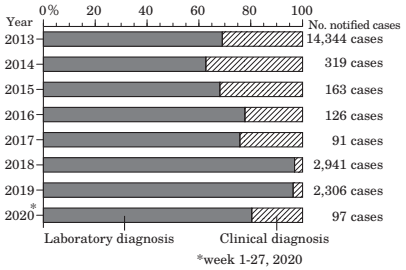
(THE TOPIC OF THIS MONTH-Continued)

Figure 3. No. and proportion of rubella cases by vaccination status, 2013-2020*, Japan
(National Epidemiological Surveillance of Infectious Diseases: as at 7 July 2020)



*week 1-27, 2020 **No. of cases < 1 year of age indicated in parenthesis ***Rubella-containing vaccine

Figure 4. No. and proportion of rubella cases by diagnosis, 2013-2020*, Japan



*week 1-27, 2020

(National Epidemiological Surveillance of Infectious Diseases: as at 7 July 2020)

against rubella, and receiving two doses makes this more certain.

CRS is also classified as a Category V Infectious Disease requiring notification of all cases based on the Infectious Diseases Control Law (http://www.niid.go.jp/niid/images/iasr/36/425/de4252.pdf). During the rubella outbreak of 2012-2014, 45 cases of CRS were reported (Fig. 1). Subsequently, there were no reports in 2015-2018, but again following a rubella outbreak, four cases were reported in 2019 and one in 2020 (as at July 7, 2020) (see p.159 of this issue).

The State of laboratory testing for rubella

In December 2017, the "Guidelines for the Prevention of Specific Infections: Rubella" were partially amended, and as of January 1, 2018, physicians are required to submit a notification upon clinical diagnosis of rubella, perform measurement of serum antibody titers, such as IgM antibody tests, and submit specimens to a local public health laboratory for detection of the rubella viral gene. Before the amendment, in 2013-2017, the percentage of cases with a laboratory diagnosis was 63-78%, which improved to approximately 95% in 2018-2019 after the amendment (Fig. 4). Due to the requirement for genetic testing for all rubella cases and the rubella epidemic, the number of laboratory tests for rubella at local public health institutes and other institutions in 2018-2019 increased considerably compared to that in 2016-2017 (see p.160 of this issue).

Facilities that conduct testing of specimens or pathogens of infectious diseases under the Infectious Diseases Control Law are required to regularly participate in external quality control assessments conducted by the national government and other organizations to ensure the reliability of testing. In the external quality control assessments conducted by MHLW in FY2018 and FY2019, the accuracy of genetic tests for measles and rubella viruses in local public health institutes was investigated, and the results were evaluated and shared (see p.161 of this issue).

National epidemiological surveillance of vaccine-preventable diseases

In FY2019, rubella hemagglutination-inhibiting antibody (HI) titers in sera collected from 5,404 healthy persons (male, n=2,724; female, n=2,680) were measured in 17 prefectures (Fig. 5). The prevalence of HI antibody titers of 1:8 or higher did not differ between males and females through their early 30s, and was generally higher than 90% from the age of two years through the early 30s. Among females, the seroprevalence was generally 90% or higher even among those in their late 30s and older persons, whereas the seroprevalence in males in their late 30s to 50s was below 90%. Seroprevalence in males born between 1962 and 1978 who are eligible for the supplementary vaccination has remained at around 80% for ten consecutive years, reflecting the presence of many susceptible individuals (see p.162 of this issue). The target date for achieving the "Additional Measures" to increase the seroprevalence level to 85% in this age group has been postponed to July 2021 due to the coronavirus disease 2019 (COVID-19) pandemic (see p.155 of this issue).

Challenges associated with rubella vaccination

To implement the "Additional Measures", males in the target age group will first receive an antibody test using the vouchers sent out by each local government. If they test negative for antibodies or have insufficient antibody titers, they will be eligible for vaccination. Even if the voucher has not been issued, it can be requested by contacting the local government. The male population eligible for this program is 15,374,162 (as at April 1, 2019), but by May 2020, only 1,740,839 (11.3% of the eligible male population) were tested for antibodies and 366,669 (2.4% of the eligible male population) were vaccinated. Therefore, MHLW is further promoting "Additional Measures", such as requesting the relevant authorities to create an environment where people can receive antibody tests for rubella in each line of work (large companies, small and medium-sized companies, self-employed persons, public servants, etc.).

A national survey of routine measles and rubella immunization rates has been conducted every year since FY 2007 (https://www.niid.go.jp/niid/ja/measles-vac.html). Routine immunization coverage against rubella in FY 2018 was 98.5% for the first dose and 94.6% for the second dose, both of which were the highest since the survey began. The target vaccination coverage of 95% or higher was achieved in all prefectures for the first dose and in 22 prefectures (47%) for the second dose. However, vaccination coverage is expected to decline in FY 2019 due to the COVID-19 pandemic. According to a study in Kawasaki City, the number of measles and rubella combination vaccines administered in March 2020 during the COVID-19 pandemic decreased to approximately 95% for the first dose and 53% for the second dose compared with the pre-pandemic period in March 2019 (see p.164 of this issue). A survey by the World Health Organization and others in June 2020 revealed that routine immunization has been suspended or discontinued in many countries, and there are concerns about outbreaks of vaccine-preventable diseases, including rubella, in the future. Even in the midst of the COVID-19 pandemic, national and local governments need to create an environment and raise awareness in order for routine vaccinations, including measles and rubella combination vaccines, to be administered as usual. Although progress has been made towards eliminating rubella and CRS globally, there are still countries where rubella-containing vaccines have not been introduced or where vaccination coverage is insufficient (see p.165 of this issue). Although the number of travelers from abroad has markedly decreased due to the COVID-19 pandemic, it is important to be prepared, to ensure that rubella virus will not spread domestically in the event of virus introduction when travel restrictions are lifted in the future.

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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