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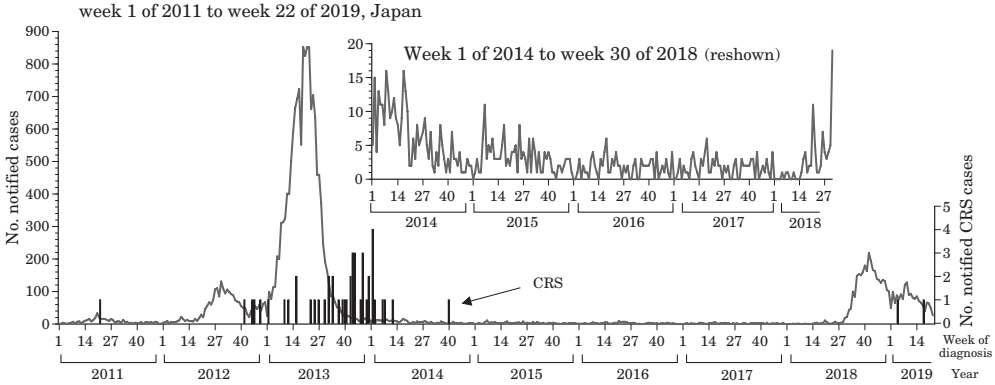
National Institute of Infectious Diseases and
Tuberculosis and Infectious Diseases
Control Division,
Ministry of Health, Labour and Welfare

<THE TOPIC OF THIS MONTH>
Rubella and congenital rubella syndrome in Japan as of May 2019

Figure 1. Weekly number of notified rubella cases and congenital rubella syndrome (CRS) cases, week 1 of 2011 to week 22 of 2019, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of 4 June 2019)

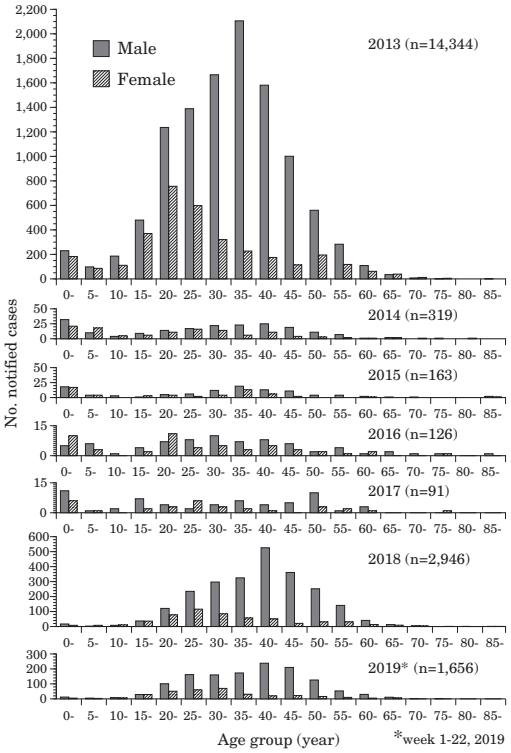
Rubella is an acute infectious disease caused by the rubella virus, and the major clinical symptoms are rash, fever, and lymphadenopathy. Rubella virus infection of pregnant women may result in prenatal transmission to the fetus and the birth of an infant with congenital rubella syndrome (CRS), which manifests as varying symptoms, including heart defects, hearing loss, and cataracts. It may lead to death in cases associated with complications such as severe heart defects (see p. 129 of this issue).

Rubella elimination is globally promoted by using the effective and safe vaccines against rubella. In 2014, the Ministry of Health, Labour and Welfare (MHLW) issued the "Guidelines for the Prevention of Specific Infections: Rubella", and set the goal of eliminating CRS in newborns as soon as possible and rubella by FY2020 in Japan. Furthermore, the guidelines were partially revised in December 2017, and further measures to control rubella were promoted such as requiring laboratory diagnosis for all suspected cases in principle. In July 2018, there was a rubella outbreak, mainly among adult males. In response to this situation, the MHLW formulated the "Immunization project for rubella" in December 2018 and decided to carry out testing for rubella-specific antibody followed by the newly scheduled routine vaccination against rubella from February 1st, 2019 to March 31st, 2022. This project targets males born between April 2nd, 1962 and April 1st, 1979 who have had no opportunity to receive routine vaccination against rubella in the past and have a lower seroprevalence of rubella-specific antibody than other generations (see p. 130 of this issue).

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

Rubella is classified as a Category V infectious disease, requiring notification of all cases (http://www.niid.go.jp/niid/images/iasr/36/425/de4251.pdf). A nationwide rubella epidemic occurred between 2012 and 2013, but the number of cases decreased between 2014 and 2017 (Fig. 1). In 2018, the number of cases increased rapidly from around week 30, mainly in the Kanto area, and 2,946 cases were notified finally. The outbreak is currently ongoing in 2019, and 1,656 cases (provisional number of notifications) have been notified by week 22 (as of May 31st, 2019).

Figure 2. Age distribution of rubella cases by gender, 2013-2019*, Japan

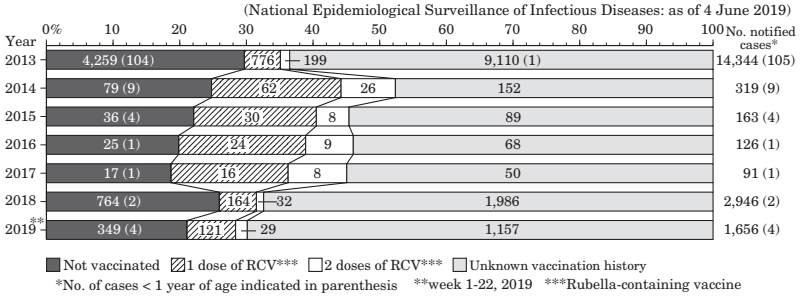


(National Epidemiological Surveillance of Infectious Diseases: as of 4 June 2019)

(Continued on page 128′)

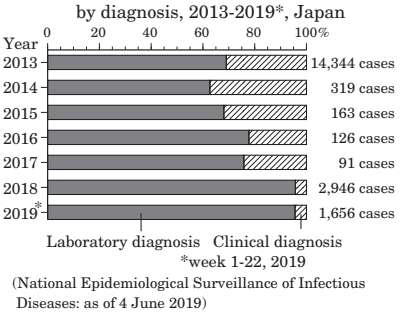
(THE TOPIC OF THIS MONTH-Continued)

Figure 3. No. and proportion of rubella cases by vaccination status, 2013-2019**, Japan



*No. of cases < 1 year of age indicated in parenthesis **week 1-22, 2019 ***Rubella-containing vaccine

Figure 4. No. and proportion of rubella cases by diagnosis, 2013-2019*, Japan



*week 1-22, 2019

(National Epidemiological Surveillance of Infectious Diseases: as of 4 June 2019)

Approximately 95% of notified patients in 2018~2019 were adults, with approximately four-times more men than women (Fig. 2 in p. 127). Although similar age and gender distributions were noted in the last epidemic in 2013, the proportion of adult male patients increased even more in 2018~2019. The median ages were 35 years for males and 26 years for females in 2013, and 41 years for males and 31 years for females in 2018. It is thought to have increased by 5 years with the passing of 5 years. In association with the large number of cases in middle-aged adult males, several rubella outbreaks in workplaces have been reported (see p. 131 of this issue).

Examining the vaccination history of rubella patients in 2013 and 2018-2019 when the number of notified cases was large, the proportion of "not vaccinated" and "unknown vaccination history" was high. On the other hand, the proportion of "1 dose of rubella-containing vaccine (RCV)" was 5-7% and "2 doses of RCV" was 1-2%, and these low proportions suggested that the epidemics are spreading among unvaccinated people (Fig. 3).

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). Accompanied by the rubella epidemic, 45 CRS cases were notified between 2012 and 2014 (Fig. 1 in p. 127). Although there were no notifications of CRS cases between 2015 and 2018, two cases were notified by week 22 of 2019 (one more case was reported in week 24 of 2019).

Laboratory testing and molecular epidemiology

As it is often difficult to diagnose rubella infection based only on clinical symptoms, it is useful to conduct laboratory tests for a reliable diagnosis. Due to the revision of the guidelines, in addition to the measurement of rubella-specific IgM antibody in serum in medical facilities, submission of specimens for detection of rubella viral genes in Prefectural and Municipal Public Health Institutes (PHIs) is now required. The proportion of laboratory diagnosis was 63-78% of all cases from 2013 to 2017 before the revision, but improved to 96% from 2018 to 2019 after the revision (Fig. 4). The increase in the rate of virological tests conducted at PHIs played a significant role in this improvement (see p. 133 of this issue). Based on genotyping data analysis of the rubella virus at PHIs, the epidemic in 2012~2013 was mainly the genotype 2B viruses, but the outbreak after week 25 of 2018 was predominantly caused by the genotype 1E rubella viruses (see p. 134 of this issue).

National Epidemiological Surveillance of Vaccine-Preventable Diseases

In FY2018, rubella hemagglutination-inhibiting antibody (HI) titers of sera collected from 5,550 healthy persons (2,875 males and 2,675 females) were measured in 17 prefectures (Fig. 5 in p. 129). The antibody positivity (HI titer ≥1:8) of both males and females aged 2 to early 30s was generally higher than 90%. In contrast, the antibody positivity of males in their late 30s to 50s was lower than 90%, which was notably lower than that of women of the same age. The seroprevalence in males born between 1962 and 1978 has remained at approximately 80% for the past 10 years, and there is still a large number of susceptible individuals (see p. 135 of this issue).

The 5th stage of routine vaccination against rubella and future measures to be taken

The newly scheduled immunization project is called "the 5th stage of the routine vaccination" because it follows the 1st and 2nd stages conducted currently, and the 3rd and 4th stages conducted between FY2008 and FY2012. As the target population is adult males with a wide range of age groups, the following three strategies have been taken in order to administer the limited measles- and rubella-combined vaccines efficiently (see p. 130 of this issue): First, antibody tests are requested before vaccination. Second, the ability to undergo antibody testing and vaccination out of one's place of residence. Third, support for concerned authorities, such as local governments and medical facilities, to carry out this program smoothly. In terms of the first strategy, only those who are antibody negative or have HI antibody titers of less than 8 are eligible for routine vaccination. Since several kits other than the HI test are also used for the measurement of rubella-specific antibody titers, the National Institute of Infectious Diseases assessed the antibody titer corresponding to an HI titer of 1:8 or less for these kits and published the data on the web site for reference (see p. 137 of this issue). The goals of the newly scheduled immunization project are "to achieve a seroprevalence of 85% in the target cohort by July 2020" and "to achieve a seroprevalence of 90% in the target cohort by the end of FY2021". To achieve this goal, it is of the utmost importance to thoroughly inform all males of the target population about the immunization project. It is also important to set up a system that makes it is easier for the target males to undergo antibody testing and vaccination, and collaboration among medical facilities, companies, and local and national governments is essential (see p. 139 of this issue). As of June 2019, the rubella antibody test based on the immunization project has been started in routine health examinations in workplaces, and it is necessary to increase its spread in the future (see p. 140 of this issue). Once a rubella outbreak occurs in a workplace, it has a significant impact on business activities (see p. 141 of this issue). From the standpoint of corporate social responsibility and business continuity, it is important to inform the companies that the additional immunization project is useful and promote awareness to make the best use of it.

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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