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<THE TOPIC OF THIS MONTH>

Rubella and Congenital Rubella Syndrome in Japan, as of June 2015

Rubella and congenital rubella syndrome (CRS) are Category V infectious diseases. Physicians who have made a diagnosis for either rubella or CRS shall notify all cases within 7 days, and preferably within 24 hours for prompt implementation of public health measures (Guidelines for the Prevention of Specific Infections: Rubella) (Ministry of Health, Labour and Welfare notice No. 122, March 28, 2014). Notification criteria are found in <http://www.nih.go.jp/niid/images/iasr/36/425/de4251.pdf> for rubella, <http://www.nih.go.jp/niid/images/iasr/36/425/de4252.pdf> for CRS; patients having all of the triad (small erythema/pink papule on the whole body, fever, and lymphadenopathy) without laboratory confirmation are classified as “clinically confirmed rubella” and those with at least one of the clinical symptoms and laboratory confirmation are classified as “laboratory-confirmed rubella”.

National Epidemiological Surveillance of Infectious Diseases (NESID)—Rubella: The reported number of rubella patients increased from a total of 378 in 2011 to 2,386 in 2012 and to 14,344 in 2013 (Fig. 1, upper panel). The reported number of rubella patients dropped to 320 in 2014. From 2011 to 2015 (through week 25), 63-78% of the reported cases were laboratory-confirmed, 80% of which were by IgM antibody detection (Fig. 1, upper panel). Although clinical diagnosis of rubella can be assisted by epidemiological information, laboratory diagnosis is strongly recommended for differential diagnosis from other infectious diseases and syndromes, such as erythema infectiosum, measles, infectious mononucleosis, enterovirus infections, streptococcal infections, and drug rash.

From 2011 to 2015 (week 25), 13,305 male and 4,214 female rubella patients (3-fold more males than females) were notified. In the 2013 epidemic, the number of male patients (664 cases) peaked in the 19th week and that of female patients (241 cases) peaked in the 21st week (Fig. 1, lower panel). In 2011, only a few prefectures, such as Fukuoka, Kanagawa and Osaka, reported relatively large number of rubella cases (Fig. 2 in p. 119 of this issue). However, in 2012, all prefectures except Ishikawa, Tokushima and Miyazaki reported cases, and in 2013, all 47 prefectures reported cases (112.7/1,000,000 population). In 2014, Tokyo and Kanagawa prefectures reported relatively large number of cases.

Among reported rubella patients, men in their early thirties and women in their early twenties were the age groups most reported in 2011-2012, while in 2013, men in their late thirties and women in their early twenties were the most reported age groups (Fig. 3). Women in their early twenties include those who were born on or prior to April 1, 1990, when a single dose was offered as routine immunization.

NESID—CRS: Women infected by rubella within 20 weeks of gestation are at risk of giving birth to CRS infants (see p. 125 of this issue). A total of 45 CRS cases were reported from week 42 of 2012 to week 40 of 2014; reports of CRS cases rose substantially

Figure 1. Weekly number of reported rubella cases and congenital rubella syndrome (CRS) cases, week 1 of 2011 to week 25 of 2015, Japan

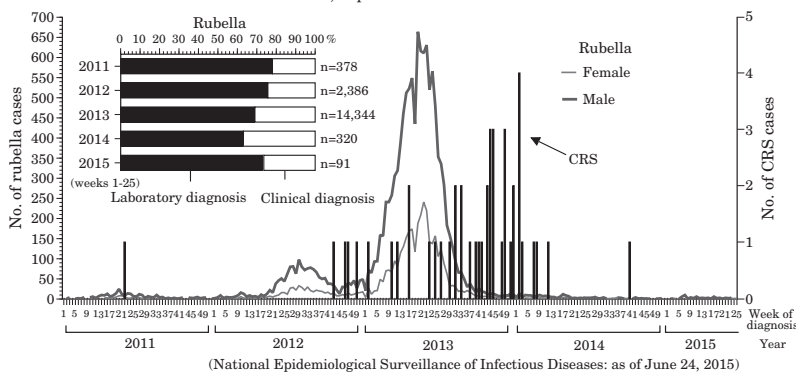
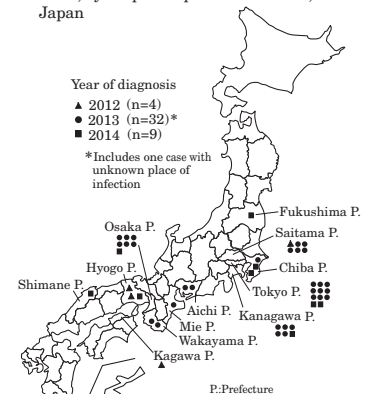


Figure 4. Number of reported congenital rubella syndrome cases, by suspected place of infection, 2012-2014, Japan



(THE TOPIC OF THIS MONTH-Continued)

(>3 cases/week) 5-6 months after the peak in reported female rubella cases (Fig. 1, lower panel). The top six prefectures with the largest number of reported CRS cases, by suspected place of infection (Fig. 4), was Saitama (6 CRS cases), Chiba (3 CRS cases), Tokyo (11 CRS cases), Kanagawa (6 CRS cases), Osaka (7 CRS cases) (see p. 120 of this issue) and Hyogo (3 CRS cases); the number of rubella cases during 2012-2013 for the respective prefectures were 704, 824, 4,116, 1,944, 3,600, and 1,455 cases (Fig. 2 in p. 119 of this issue).

Follow-up testing of throat swabs of 12 CRS infants revealed that the rubella virus frequently persisted for three months but up to 13 months after birth (see p. 120 of this issue). As newborns without any signs or symptoms may develop hearing loss (see p. 123 of this issue) or cataract later, infants born to mothers infected or suspected to be infected with rubella require careful monitoring.

Routine immunization coverage: As of May 2015, two doses of measles-rubella (MR) combined vaccine are provided as routine immunization, with the first dose at one year of age and the second dose within 1 year prior to primary school entrance. During fiscal year 2011 to 2013, the vaccination coverage was 95.3-97.5% for the first dose and 92.8-93.7% for the second dose (see p. 132 of this issue).

Rubella seropositivity in the population (National Epidemiological Surveillance of Vaccine-Preventable Diseases): In 2014, 17 prefectural and municipal public health institutes (PHIs) in Japan surveyed 5,743 healthy individuals (2,882 males and 2,861 females) for rubella hemagglutination inhibition (HI) antibody level (Fig. 5 in p. 119 of this issue). The proportion seropositive (≥ 8 HI titers) was 25-27% in infants <1 year of age, 63-67% in one year olds, and $\geq 90\%$ among those 2-29 years of age (93% in males and 96% in females). The proportion seropositive was $\geq 90\%$ for female adults in all age groups, but varied among male adults (82% for 35-39 years, 79% for 40-44 years, 74% for 45-49 years, and 77% for 50-54 years) (see p. 130 of this issue). This gender difference is due to the fact that only women received routine rubella vaccination among those born between April 2, 1962 and April 1, 1979.

Rubella epidemics overseas and virus genotypes: Globally, many countries in the world repeatedly experience large scale rubella epidemics, and WHO estimates that 110,000 CRS infants are born annually. The World Health Assembly in 2012 adopted the resolution to eliminate rubella by 2020 in five of the six WHO regions, and the Americas region was the first to attain this goal, in April 2015.

There are currently 13 known genotypes for rubella virus. From 2011 to June 2015, globally circulating genotypes were 1a, 1E, 1G, 1J and 2B; notably, genotype 2B had spread globally since 2006. Genotypes prevalent in the WHO's Western Pacific and Southeast Asian Regions are 1E and 2B. As the number of circulating genotypes has recently declined, phylogenetic analysis of the isolates is becoming necessary for tracing the movement of rubella virus (see p. 135 of this issue).

Challenges and next steps: Japan aims to eliminate rubella by 2020 and achieve zero CRS cases. Special guidelines outlining the necessary activities are now available (see p. 133 of this issue). The 2013 rubella epidemic (IASR 34: 348-349, 377-378, 2013 & 35: 17-19, 2014), however, revealed the persistence of large number of susceptible male adults in Japan. Thus, without intervention in this population, achieving such goals will be difficult. As the most frequent place for rubella transmission was the workplace during the 2013 epidemic, the role of companies, particularly their occupational physicians at the workplace, needs to be emphasized (see p. 128 of this issue). The Day Care Division of Equal Employment, Children and Families Bureau, MHLW, recommends conducting rubella antibody tests or vaccination to trainees at nursing training facilities who do not have a history of rubella infection or vaccination (see p. 134 of this issue).

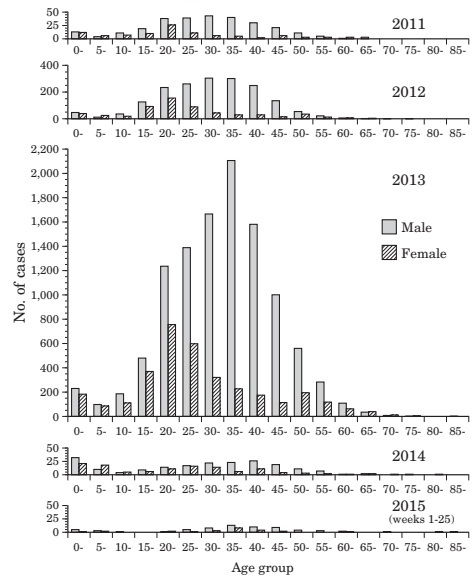
The National Institute of Infectious Diseases has produced guidelines on i) rubella prevention in the workplace, ii) rubella prevention in medical settings, iii) local government's response to rubella outbreaks, iv) establishment of committees and other measures for rubella control at the prefectural level, and v) guidelines for the notification of rubella and CRS for medical doctors.

Elimination of rubella by 2020 requires the concerted efforts of relevant stakeholders, and each and every person should work towards this goal. The following measures should be taken:

1. Communicate that the risk of CRS can be prevented by vaccination not only to women expecting pregnancy and their family but also to unmarried men and women. Higher accessibility to antibody testing and MR vaccination to this population should be attained (see pp. 120, 122 & 129 of this issue).
2. Consultation services concerning CRS should be provided to physicians in primary obstetric facilities; currently 16 secondary obstetric facilities in the nine prefectural blocks in Japan provide such services (see p. 122 of this issue).
3. Post-delivery vaccination to women with rubella HI antibody ≤ 16 .
4. In the case of an outbreak involving a company, there should be cooperation between the affected company and regulators. In fact, when rubella emerged in a company that had branches in Asian countries, collaboration between the company, the local health centers, and the local government successfully prevented further expansion of the outbreak in 2015 (see p. 126 of this issue).

It should be reminded that MR vaccination without prior antibody testing does not cause any harm. What should be avoided is to neglect follow-up of people found to lack antibody against rubella.

Figure 3. Age distribution of rubella cases by gender, 2011-2015, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of June 24, 2015)

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 Law Concerning the Prevention of Infectious Diseases and Medical Care for Patients of Infections, and 2) other data covering various aspects of infectious diseases. The prefectural and municipal health centers and public health institutes (PHIs), the Department of Food Safety, the Ministry of Health, Labour and Welfare, and quarantine stations, have provided the above data.

(特集つづき)

図2. 都道府県別風疹患者発生状況, 2011~2014年
Figure 2. Number of reported rubella cases and notification rate, by prefecture, 2011-2014, Japan

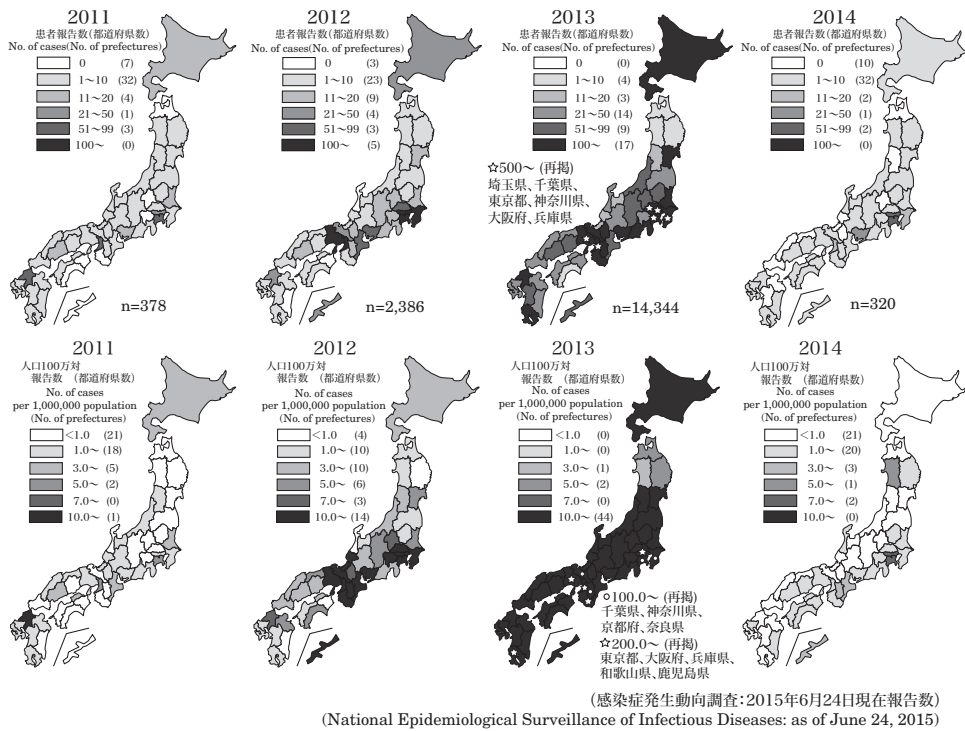
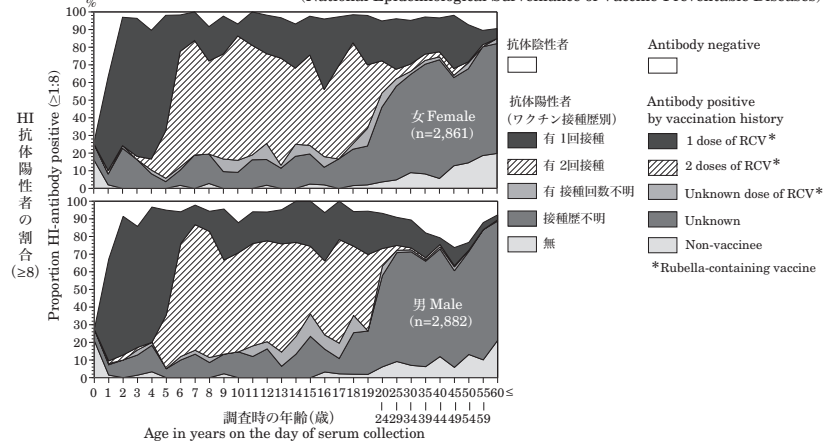


図5. 年齢別風疹抗体保有状況, 2014年(感染症流行予測調査)
Figure 5. Proportion seropositive against rubella virus by age and gender, 2014, Japan
(National Epidemiological Surveillance of Vaccine-Preventable Diseases)



— 参考URL —

- ・ 風しんに関する特定感染症予防指針
<http://www.mhlw.go.jp/file/06-Seisakujouhou-10900000-Kenkoukyoku/0000041928.pdf>
- ・ 感染症発生動向調査風疹届出基準
風しん: <http://www.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou11/01-05-14-02.html>
先天性風しん症候群: <http://www.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou11/01-05-10.html>
- ・ 風疹対策ガイドライン(感染研)
 - ① 職場における風しん対策ガイドライン
<http://www.nih.go.jp/niid/images/idsc/disease/rubella/kannrenn/syokuba-taisaku.pdf>
 - ② 医療機関における風しん対策ガイドライン
<http://www.nih.go.jp/niid/images/idsc/disease/>

- http://www.nih.go.jp/niid/images/epi/rubella/rubella_gl_150310.pdf
- ③ 自治体における風しん発生時対応ガイドライン〔第一版〕
http://www.nih.go.jp/niid/images/epi/rubella/rubella_gl_150310.pdf
- ④ 都道府県における麻しん風しん対策会議等に関するガイドライン〔第一版〕(旧「都道府県における麻しん対策会議等に関するガイドライン」より改訂)
http://www.nih.go.jp/niid/images/epi/rubella/GLMM_150310.pdf
- ⑤ 医師による風しん・先天性風しん症候群届出ガイドライン(第1版)
http://www.nih.go.jp/niid/images/epi/rubella/RubellaCRS_GL_20150327.pdf