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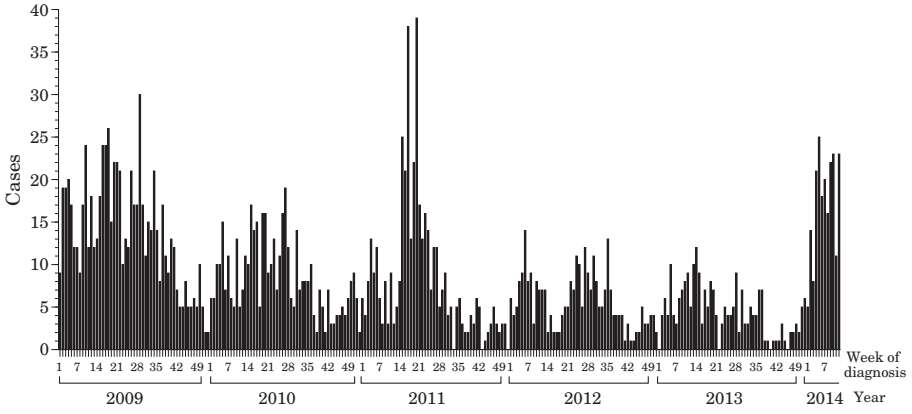
National Institute of Infectious Diseases and
Tuberculosis and Infectious Diseases
Control Division,
Ministry of Health, Labour and Welfare

<THE TOPIC OF THIS MONTH>
Measles in Japan, as of March 2014

Figure 1. Weekly number of reported measles cases, week 1 of 2009 to week 12 of 2014, Japan

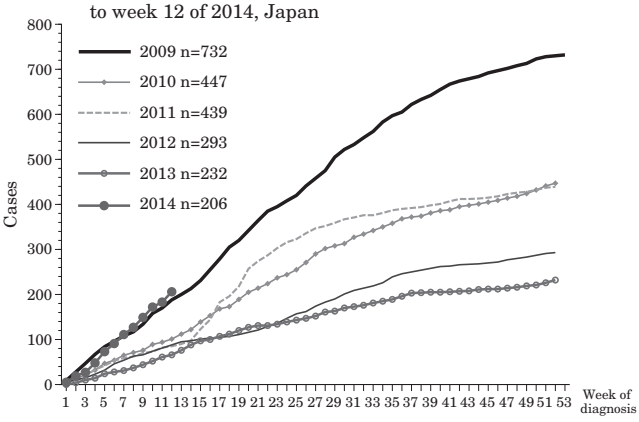


(National Epidemiological Surveillance of Infectious Diseases: as of March 26, 2014)

Measles is characterized by high fever, general exanthema and prodromal catarrh symptoms (notification criteria http://www.nih.go.jp/niid/images/iasr/35/410/de4101.pdf). Severe complications include pneumonia and encephalitis.

In response to the massive outbreak in 2007 that mainly affected those aged 10-20 years, the Ministry of Health, Labour and Welfare announced the "Special Infectious Disease Prevention Guidelines on Measles" (Prevention Guideline in short) on December 28, 2007 (see p. 96 of this issue). In April 2013, the Prevention Guideline was revised to include an objective, "accomplishing measles elimination by 2015 to obtain measles elimination verification from WHO and maintaining the elimination status thereafter".

Figure 2. Cumulative number of measles cases by week, week 1 of 2009 to week 12 of 2014, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of March 26, 2014)

Measles incidence under the National Epidemiological Surveillance of Infectious Diseases: Largely owing to the catch-up immunization conducted in 2008-2012 targeting age groups corresponding to children in the 1st year of junior high school and those in the 3rd year of high school (IASR 33: 27-29, 2012), measles incidence decreased steadily (Fig. 1) (see also http://idsc.nih.go.jp/iasr/33/384/graph/f3841.gif). In 2013, despite the large measles outbreak in China and other Western Pacific countries (see p. 97 of this issue), the incidence in Japan was the lowest since the start of notification of all measles cases (Fig. 2), i.e., 232 in total or 1.8 per million population.

Since October 2013, however, measles incidence has been increasing in various locations in Japan. Most cases were imported from or associated with cases from the Philippines (see pp. 98, 102 & 103 of this issue). In 2014, the total number of patients notified from week 1 to week 12 was 206 (as of March 26, 2014), which was the highest number of reported cases for the same corresponding period during the past 6 years (Fig. 2). Suspected nosocomial transmissions have been reported in various locations (see pp. 105, 107 & 108 of this issue). Owing to prompt measures including vaccinations, large-scale measles outbreaks have been avoided so far.

As for measles encephalitis, a one-year-old case was reported in 2013 and an adult case (30's) case has been reported in 2014 as of the 12th week.

In 2013, notifications from the Tokyo metropolitan area, Saitama, Kanagawa and Chiba prefectures occupied 64% of all notified cases; the largest number of cases were reported from Tokyo (67 cases) followed by Kanagawa (34 cases), Saitama (27 cases), Aichi

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(THE TOPIC OF THIS MONTH-Continued)

(24 cases) and Chiba (20 cases) prefectures. In 2013, 35 prefectures (in contrast to 32 prefectures in 2012, 19 prefectures in 2011) reported less than one case per million population (WHO's measles elimination indicator, IASR 32: 34-36, 2011), among which 28 prefectures reported no case. As of week 12 of 2014, Tokyo has reported 34 cases, Shizuoka 23 cases, Chiba 22 cases, Kyoto 21 cases and Saitama 18 cases.

As for age distribution (Fig. 3 in p. 95), those older than 20 years occupied nearly 70% of the reported cases; those aged 10-19 years, who made up 43% of reported cases in 2008, was reduced to 6%, indicating the likely success of the vaccination program in recent years. From the beginning of 2014, however, patients <20 years of age have been increasing, and, as of the 12th week, 57% of reported cases were of this age group. The male-to-female ratio so far in 2014 is 1:1 in contrast to 3:2 in 2013.

Among the 232 measles patients notified in 2013, 52 (22%) had received no vaccination, 51 (22%) one dose and 9 (4%) two doses. The vaccination status of the remaining 120 cases (52%) was unknown. All cases less than one year of age had not received vaccination. Among 163 cases older than 20 years of age, 21 (13%) had received no vaccination and the vaccination status for the 111 (68%) were unknown.

Among the 206 measles cases notified up to week 12 of 2014, there were 113 unvaccinated cases (55%), 31 cases with one dose, 13 cases with two doses and 49 cases with unknown vaccination status. So far in 2014, the proportion unvaccinated among measles cases, has been the highest since 2008 (Fig. 4 in p. 95).

As for school closure due to measles, while there were none in 2013, in 2014 a high school and a primary school were closed in January and in February, respectively.

Isolation and detection of measles virus: The measles virus genotype D5 that had been endemic in Japan during 2006-2008 has not been detected in Japan since May 2010. Thereafter, all isolates had genotypes of foreign origin, such as D9, G3, D8, D4 and H1 (Fig. 5 in p. 95). In 2013, a B3 strain was isolated for the first time in Japan from a patient who returned from Thailand (IASR 34: 201-201, 2013). In 2013, genotype B3 was the most frequent genotype detected (n=26), followed by D8 (14 cases), H1 (5 cases) and D9 (5 cases). Although direct epidemiological links could not be identified, multiple genotype D8 cases were reported from several prefectures from July to August, and were believed to have been part of the same outbreak (see p. 100 of this issue).

From the beginning of 2014, genotype B3 has been increasingly detected from those who returned from the Philippines (see pp. 98 & 102 of this issue), and as of April 1, 139 cases have been notified. Other genotypes detected so far are D8 (9 cases), D9 (6 cases) and H1 (2 case), with 3 cases unknown.

Laboratory diagnosis and its importance: The Prevention Guideline recommends i) earliest notification possible, followed by ii) prompt laboratory diagnosis, and iii) withdrawal of the notification if measles is denied by laboratory tests. It is thus possible that some of the 61 clinically diagnosed cases in 2013 were those whose laboratory test had not yet been completed. New IgM test kits commercialized in 2014 show little false positivity to the acute phase of erythema infectiosum (a human parvovirus B19 infection) and other exanthema diseases. Importantly, measles virus infection can be detected by PCR or virus isolation only within 7 days after rash appearance (though measles virus may persist in urine longer than 7 days and can be detected by PCR; see "Principles of Laboratory Diagnosis, revised in 2014) and by IgM from 4 to 28 days after rash appearance. Results need to be interpreted with caution as specimens collected too early or too late can falsely show negative results.

The National Epidemiological Surveillance of Vaccine-Preventable Diseases (see p. 109 of this issue): WHO considers that measles elimination requires 95% population immunity against measles virus in every birth cohort. In FY2012, the antibody-positivity level (gelatin particle agglutination (PA) assay >1:16) became ≥95% in all age groups aged 2 years or above, and similarly in FY2013, levels were maintained for majority of age groups 2 years or older (Fig. 6 in p. 95). Seventy-six percent of one year old children were antibody positive in FY2013 (67% in FY2012).

Vaccination coverage: Since FY2006, routine immunization policy in Japan has adopted measles-rubella combined vaccine (MR), which has been administered in two doses, the first dose at one year of age (1st vaccination) and the second dose to children the year prior to elementary school attendance (2nd vaccination) (IASR 27: 85-86, 2006). In addition, from FY2008 to FY2012, supplementary vaccination was conducted to children whose age corresponded to the age of the first year of junior high school (3rd vaccination) and third year of high school (4th vaccination) to also ensure two doses in these age groups (IASR 29: 189-190, 2008).

For FY2012, the vaccination coverage of measles-containing vaccines (M, MR) (the denominator for the 1st vaccination: number of 1-year-old babies as of October 1, 2012; the denominator for the 2nd-4th vaccinations: respective number of eligible age groups as of April 1, 2012) was 98% (95% in FY2011), 94% (93% in FY2011), 89% (88% in FY2011), and 83% (81% in FY2011) respectively for the 1st, 2nd, 3rd and 4th vaccinations. The 1st vaccination covered ≥95% of the eligible children, fulfilling the target of sustaining this level for three successive years. However, the coverage of the 2nd vaccination in the first half of FY2013 was lower than that in FY2012 in 36 prefectures.

Measures to be taken: Since the end of 2013, small-scale outbreaks due to imported measles, mainly of genotype B3, have been increasing, involving medical facilities or families in various parts of Japan. More than 50% of the patients were unvaccinated children under 10 years of age. Medical practitioners should include measles in the differential diagnosis even during influenza or rubella seasons. They should pay attention to travel history abroad and vaccination history. Once measles infection is suspected, immediate infection control measures should be taken. Healthcare workers should ensure that they have received two doses of measles-containing vaccine.

Since early March this year, measles cases without history of travel abroad are increasing in number. In order to contain measles which historically peak from spring to summer, all patients suspected of measles should be epidemiologically investigated with laboratory follow-up. To this end, medical facilities should closely coordinate with health centres, prefectural and municipal public health institutes and the National Institute of Infectious Diseases. So as not to import measles from abroad, vaccination should be completed before travelling overseas.

In order to interrupt measles transmission in Japan, high vaccination coverage should be maintained so transmission would not be sustained even if there is importation of the virus. And, active epidemiological investigation and appropriate preventive measures should be taken following the "one suspected case, immediate response" principle.

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.

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（特集つづき）

図3. 麻疹患者の年齢分布，2008～2014年*
Figure 3. Age distribution of measles cases, 2008-2014*, Japan

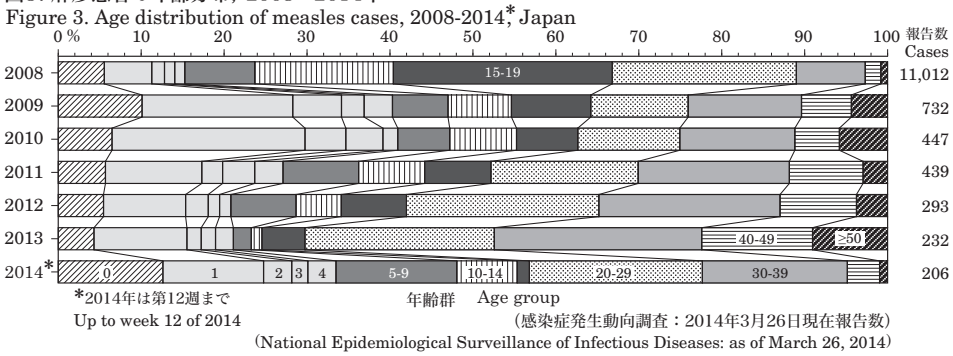

図4. 麻疹患者の予防接種歴別割合，2008～2014年*
Figure 4. Percentage of measles cases by vaccination status, 2008-2014*, Japan

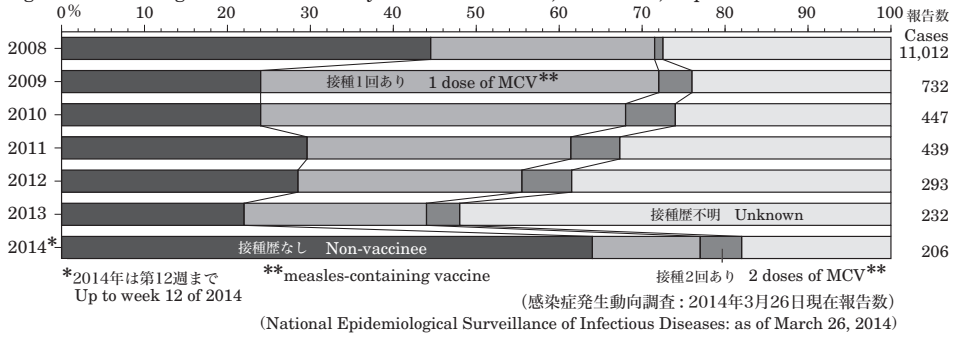

図5. 月別麻疹ウイルス分離・検出報告数，2008年1月～2014年3月
Figure 5. Monthly number of reported measles cases with virus isolation/detection by genotype, January 2008-March 2014, Japan （病原微生物検出情報：2014年4月1日現在報告数）

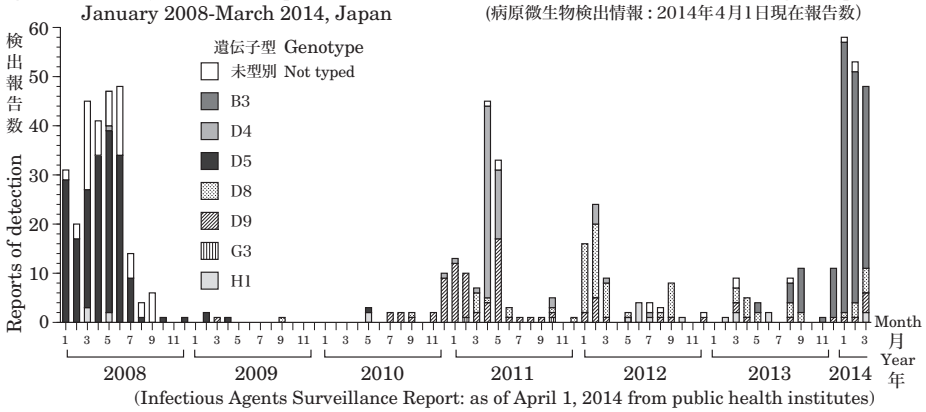

図6. 年齢別麻疹抗体保有状況，2013年度（感染症流行予測調査）（ゼラチン粒子凝集法：PA法）
Figure 6. Proportion seropositive against measles virus by age and vaccination status, fiscal year 2013 (April 2013 to March 2014), Japan (Particle agglutination assay)
(National Epidemiological Surveillance of Vaccine-Preventable Diseases)