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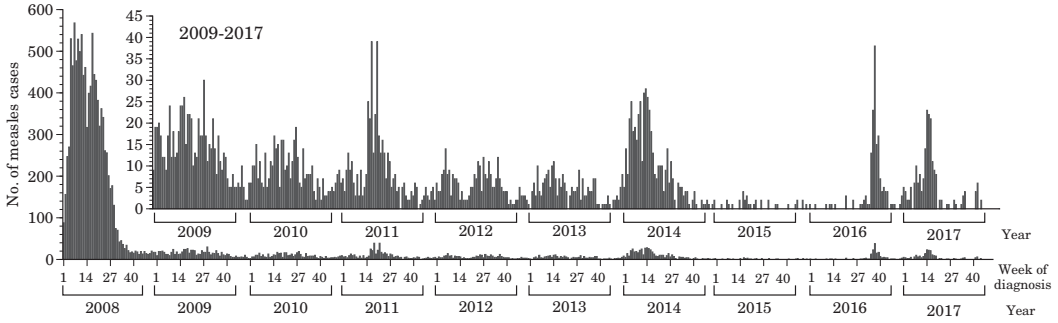
National Institute of Infectious Diseases and
Tuberculosis and Infectious Diseases
Control Division,
Ministry of Health, Labour and Welfare

<THE TOPIC OF THIS MONTH>
Measles in Japan, as of February 2018

Figure 1. Weekly number of reported measles cases, 2008-2017, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of March 2, 2018)

Measles is an acute infectious viral disease characterized by three main clinical manifestations of fever, rash, and catarrh. The measles virus, the causative agent of measles, is transmitted as an aerosol, droplet, or via contact and is highly infectious. As it also transiently suppresses the host's immune function, approximately 30% of measles case patients suffer from complications, and those who develop pneumonia or encephalitis can have fatal outcomes. In 2016, an estimated 89,780 persons, mainly children in developing countries, died of measles (http://www.who.int/mediacentre/factsheets/fs286/en/).

Measles is considered to be an infectious disease that can be eradicated due to the following criteria: 1) humans are the sole reservoir for the measles virus; 2) accurate laboratory tests for the virus exist; and 3) effective, economical vaccines are available. Following the eradication of smallpox, the World Health Organization (WHO) aims to eradicate poliomyelitis and measles. In 2005, the Regional Committee of the WHO Western Pacific Region (WPR), the region that includes Japan, resolved to eliminate measles from the WPR by 2012. In response, a two-dose vaccination schedule for measles-containing vaccines was introduced in Japan in 2006. Around that time, as measles epidemics mainly involved adolescents, the Japanese Ministry of Health, Labour and Welfare issued the "Guidelines for the Prevention of Specific Infectious Diseases: Measles" (hereafter referred to as the guidelines) in December 2007 and took various countermeasures against measles, such as 1) implementing a catch-up immunization program, which targeted age groups corresponding to the 1st grade of junior high school and the 3rd grade of high school, to enhance immunity against measles among adolescents (a 5-year time-limited measure), and 2) changing the reporting system for measles from sentinel surveillance to notifiable disease surveillance to strengthen measles surveillance. In addition, the 2013 revision of the guidelines stated that, as a rule, laboratory IgM tests and detection of the measles virus genome (i.e., PCR) should be carried out for all suspected measles cases–this is in order to investigate the origin and transmission route of the circulating measles virus, requirements for measles elimination. These measures led to a reduction in the number of measles cases and the absence of endemic virus transmission for ≥12 months in Japan. As a result, the Regional Verification Committee of the WPR verified in March 2015 that Japan had achieved measles elimination, and this status has been maintained to this day (see p. 60 of this issue).

Measles notifications under the National Epidemiological Surveillance of Infectious Diseases (NESID) system: Measles is a category V infectious disease according to the "Act on the Prevention of Infectious Diseases and Medical Care for Patients with Infectious Diseases" (Infectious Diseases Control Law) (http://www.niid.go.jp/niid/images/iasr/35/410/de4101.pdf).

The number of reported measles cases in Japan was 11,013 in 2008, when measles became a notifiable disease surveillance started, but it has declined since 2009, with annual notifications ranging from 35 to 732 cases.

In 2017, a total of 187 cases of measles were reported (as of March 2, 2018). These included outbreaks that involved more than 10 cases, namely the outbreak that predominantly affected Yamagata Prefecture (60 cases) (see p. 54 of this issue), the outbreak in Mie Prefecture (see p. 52 of this issue), and the outbreak in Hiroshima Prefecture (see p. 53 of this issue); there were also outbreaks that terminated without tertiary transmissions (see pp. 55&57 of this issue) (Fig. 1).

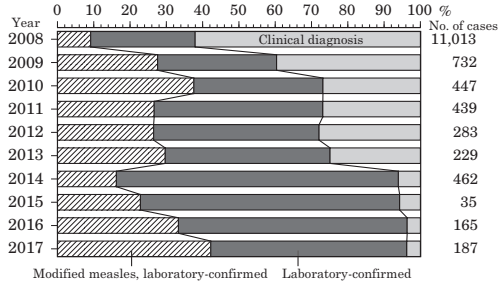
As for the disease classification (Fig. 2 in p.50), the proportion of modified measles, i.e., laboratory confirmed measles that is atypical in presentation with only one or two of the three main signs of typical measles, has been increasing since 2014, and modified measles accounted for 42.2% (79/187) of reported measles cases in 2017.

Regarding the age distribution (Fig. 3 in p.51), measles used to be an infectious disease that primarily affected children under 5 years of age; however, in 2008, when measles became a notifiable disease, a measles epidemic that mostly involved adolescents and young adults occurred. At this time, 66.7% of all measles cases involved patients aged ≤19 years (10-19 years: 43.1%; children under 10 years: 23.6%). Afterwards, thanks to activities such as the catch-up vaccination program for junior high school and high school students, the proportion of measles cases ≤19 years of age declined, decreasing to 19.2% in 2017. In contrast, adults 20 years of age or

(Continued on page 50′)

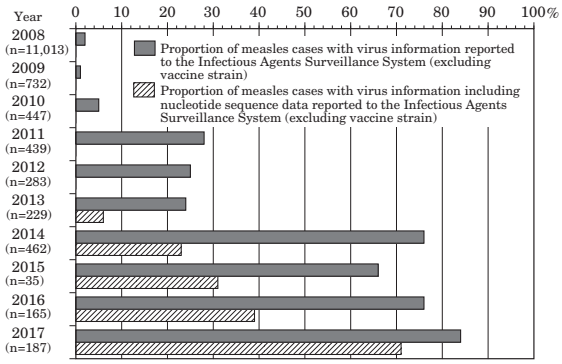
(THE TOPIC OF THIS MONTH-Continued)

Figure 2. Distribution of measles cases by disease classification, 2008-2017, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of March 2, 2018)

Figure 4. Reporting status of measles virus information by PHIs to the Infectious Agents Surveillance System, 2008-2017, Japan



(Infectious Agents Surveillance System: as of March 2, 2018)
(National Epidemiological Surveillance of Infectious Diseases: as of March 2, 2018)

older have accounted for >70% of cases since 2015, and reached 80.7% in 2017.

Among the 187 measles cases reported in 2017, 33 (17.6%) were unvaccinated, and 3 were <1 year of age (9.1% of unvaccinated individuals) and had not reached the age at which routine vaccination is performed; 49 (26.2%) had received 1 dose, 21 (11.2%) had received 2 doses, and 84 (44.9%) had unknown vaccination history (Table 1 in p.51). The annual number of measles cases has remained low (ranging from 35 to 187 cases) since 2015, with a decline in the proportion of unvaccinated individuals and increase in the proportion of vaccinated individuals. This is considered to be related to aspects such as the following: 1) the number of vaccinated individuals has been increasing, and 2) milder and atypical cases of measles are becoming diagnosed as measles or modified measles due to the implementation of active epidemiological investigations and PCR-based detection of the measles virus. In addition, the risk of infection from modified measles appeared to be lower than that from typical measles (see p. 59 of this issue).

There has been no emergency school closure due to measles since the temporary closure of a primary school in February 2014 (http://www.nih.go.jp/niid/ja/hassei/5339-measles-school-rireki.html).

Detection of measles virus: In 2017, prefectural and municipal public health institutes (PHIs) reported 166 measles cases whose measles virus genome was detected, and reported the data through the Infectious Agents Surveillance System, NESID's laboratory surveillance system. After excluding the cases detected with the vaccine strain, there were 158 such cases (84.5% of the total 187 measles cases). Among these 158 cases, the genotype of the virus was analyzed in 150 cases (80.2% of the total 187 cases), and the nucleotide sequence of the measles virus was also reported in 132 cases (70.6% of the total 187 cases) (Fig. 4). The epidemiological situation recorded was as follows: 75 sporadic cases, 65 outbreak cases, 14 familial cases, and 5 local cases. Among the 158 cases, 36 (23%) were cases that had travelled abroad. Regarding genotype, genotype D8 was the most frequent with 140 cases, and for those with a history of travelling abroad before disease onset, countries such as Indonesia, Thailand, and India were reported. The next most frequent was genotype B3 with 8 cases, and 6 of these involved cases that had a history of overseas travel (destinations: Italy, Gabon, Singapore, Pakistan, and Bangladesh). Genotype H1 was detected in 2 cases, in which the cases had travelled to Vietnam and Myanmar, respectively. There were 8 cases in which the genotype was unknown (Table 2 in p.51).

Current practice regarding laboratory diagnosis: As PCR-based tests have high sensitivity for detecting measles in the early phase after onset and can be used to infer the place of origin and transmission routes of the measles virus, their importance have increased after achieving measles elimination.

In order to minimize potential false-positives due to cross-contamination during PCR-based tests, it is recommended that real-time reverse transcription (RT)-PCR should first be used to detect the virus genome (for diagnosis), and if the result is positive, to perform conventional RT-PCR (nested RT-PCR) for sequence analysis of the genotyping region on the N gene of the measles virus genome. In addition, using the 3 specimens composed of a throat swab and blood and urine samples is encouraged.

Vaccination coverage: Since FY2006, the measles-rubella combined vaccine has been used in the routine immunization program in Japan. The following vaccination schedule was introduced in 2006 and is still used: the 1st dose of the vaccine is administered at 1 year of age, and the 2nd dose is administered during the year before primary school entry. In FY2016, the vaccination coverage for the 1st dose was 97.2%, and that for the 2nd dose was 93.1%. The coverage for the 1st dose has been ≥95% for the past 7 years. Although the coverage for the 2nd dose has been ≥90% for the past 9 years, efforts at achieving the 95% target are still ongoing (https://www.niid.go.jp/niid/images/idsc/disease/measles/2016-mr-pdf/2016_map.pdf).

National Epidemiological Surveillance of Vaccine Preventable Diseases (NESVPD): In FY 2017, the NESVPD measles seroprevalence survey was conducted at the PHIs in 23 prefectures using the gelatin particle agglutination (PA) assay (n=6,247) (see p. 61 of this issue). In general, the blood collection period ran from July 2017 to September 2017. The proportion of antibody-positive (a PA titer of ≥16) individuals aged ≥2 years in this population has been ≥95% for all age groups since FY 2011 (Fig. 5 in p.51).

Further measures to be taken: Measles is still occurring in many countries overseas (see pp. 62&66 of this issue). As a total of 45 million people enter and leave Japan each year, it is difficult to completely prevent the entry of measles virus from abroad. Under such conditions, it is important that measles does not spread further following its importation. In order to achieve this, the following are requested: 1) to ensure the administration of 2 doses of the routine vaccine (each at a coverage rate of ≥95%) to maintain a high antibody positivity level among the general population; 2) to strengthen surveillance in order to ensure rapid detection of a case and implement appropriate response to prevent further spread; and 3) to encourage people who are at high risk of measles infections, such as healthcare workers, those who work at schools or in childcare, overseas travelers, those who work at locations such as airports where they come into contact with large numbers of people, and cohorts who have only received one dose of the measles vaccine, to get vaccinated. In addition, it is also important to coordinate with international organizations, such as the WHO, to support global measles control (see p. 64 of this issue).

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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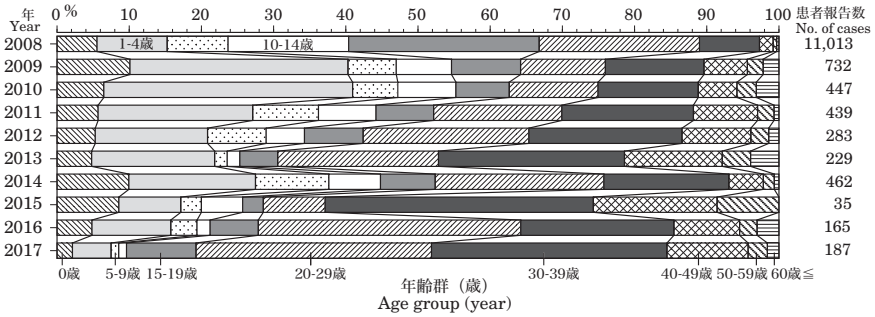
(特集つづき) (THE TOPIC OF THIS MONTH-Continued)

図3. 麻疹患者の年齢分布, 2008～2017年

Figure 3. Age distribution of measles cases, 2008-2017, Japan



(感染症発生動向調査：2018年3月2日現在報告数)

(National Epidemiological Surveillance of Infectious Diseases: as of March 2, 2018)

表1. 麻疹患者の予防接種歴別報告数, 2008～2017年

Table 1. Number of measles cases by vaccination status, 2008-2017, Japan

年 Year	接種歴なし Non-vaccinee	1回接種 1 dose of MCV**	2回接種 2 doses of MCV	接種歴不明 Unknown	患者報告数* No. of cases*
2008	4,914 (590)	2,933 (12)	132	3,034 (9)	11,013 (611)
2009	173 (73)	349	31	179 (1)	732 (74)
2010	108 (29)	193	29	117	447 (29)
2011	130 (25)	139	26	144	439 (25)
2012	79 (15)	76	17	111	283 (15)
2013	52 (11)	50	9	118	229 (11)
2014	216 (43)	87 (3)	32	127	462 (46)
2015	16 (3)	6	0	13	35 (3)
2016	47 (7)	40	25	53 (1)	165 (8)
2017	33 (3)	49 (1)	21	84	187 (4)

*うち( )は0歳　(感染症発生動向調査：2018年3月2日現在報告数)

*No. of cases < 1 year of age indicated in parenthesis.　**Measles-containing vaccine

(National Epidemiological Surveillance of Infectious Diseases: as of March 2, 2018)

表2. 麻疹ウイルス検出例の発生の状況と渡航歴と渡航先, 2017年

Table 2. Measles virus isolation/detection by epidemiological situation, travel history and destination abroad, 2017

遺伝子型 Genotype	例数 No. of cases	発生の状況† Epidemiological situation† 散発 Sporadic	家族内発生 Familial	地域流行 Local	集団発生 Outbreak	渡航歴 無／不明 No/unknown travel history	渡航歴 有 Overseas travel history	渡航先* Destination abroad* イタリア Italy	インド India	インドネシア Indonesia	ガボン Gabon	カンボジア* Cambodia*	シンガポール Singapore	タイ* Thailand*	ネパール Nepal	パキスタン Pakistan	バングラデシュ Bangladesh	ベトナム Viet Nam	マレーシア Malaysia	ミャンマー Myanmar
合計 Total	158	75	14	5	65	122	36	2	3	15	1	1	1	8	1	1	1	1	1	1
Not typed	8	3	-	-	5	8	-	-	-	-	-	-	-	-	-	-	-	-	-	-
B3	8	5	3	-	-	2	6	2	-	-	1	-	1	-	-	1	1	-	-	-
D8	140	65	11	5	60	112	28	-	3	15	-	1	-	8	1	-	-	-	1	-
H1	2	2	-	-	-	-	2	-	-	-	-	-	-	-	-	-	-	1	-	1

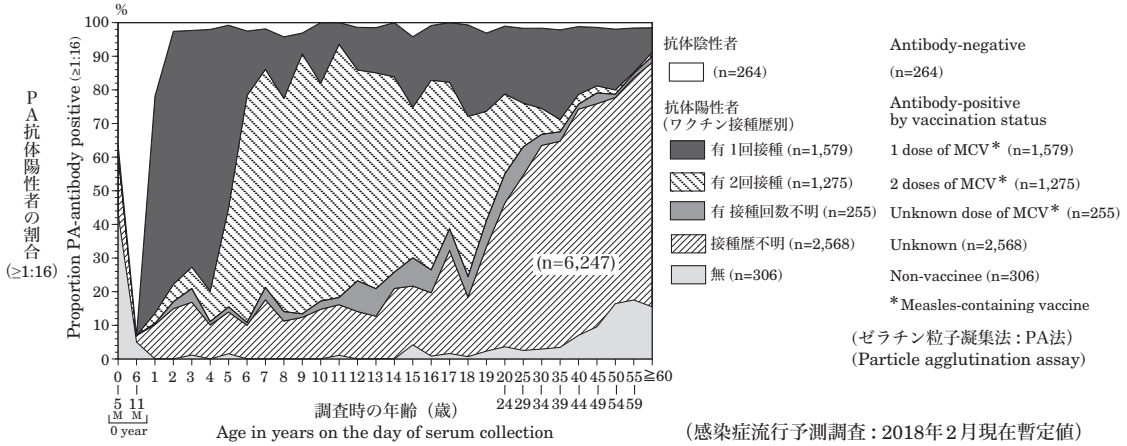
†重複あり　*2つ以上の国へ渡航した例を含む　(病原微生物検出情報：2018年2月15日現在報告数)

†May be categorized under more than one situation. *Includes a case who visited more than one country

[Infectious Agents Surveillance System: as of February 15, 2018 from prefectural and municipal public health institutes (PHIs)]

図5. 年齢別/年齢群別麻疹抗体保有状況, 2017年度

Figure 5. Proportion seropositive against measles virus by age and vaccination status, fiscal year 2017, Japan



(感染症流行予測調査：2018年2月現在暫定値)

(National Epidemiological Surveillance of Vaccine-Preventable Diseases: as of February, 2018)