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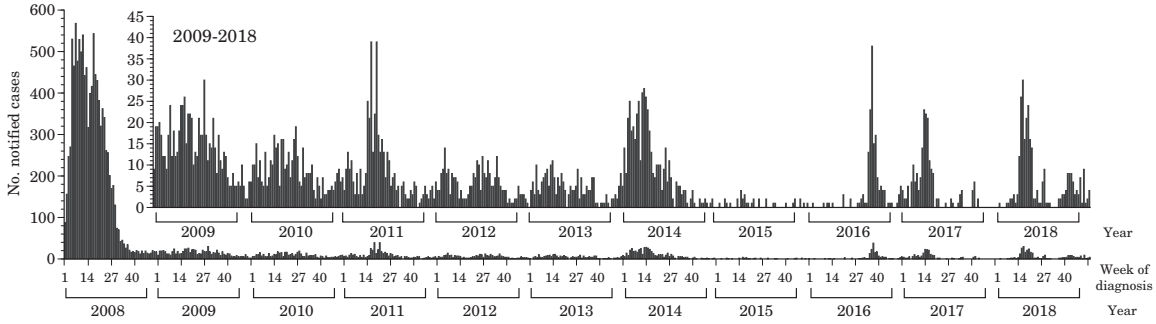
National Institute of Infectious Diseases and
Tuberculosis and Infectious Diseases
Control Division,
Ministry of Health, Labour and Welfare

<THE TOPIC OF THIS MONTH>
Measles in Japan, as of February 2019

Figure 1. Weekly number of notified measles cases, 2008-2018, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of 28 February 2019)

Measles is an acute infectious disease caused by the measles virus. The main clinical manifestations are fever, rash, and catarrh. The measles virus is transmitted as an aerosol, droplet or by contact, and its infectivity is markedly high. Measles patients frequently develop complications and may die if they develop pneumonia or encephalitis. Although it is rare, those who have caught and recovered from measles can develop subacute encephalitis with a poor prognosis known as subacute sclerosing panencephalitis (SSPE) several to 10-odd years after recovery (see p. 52 of this issue). The World Health Organization (WHO) estimated that 109,638 people, mainly children in developing countries, died from measles in 2017 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6276384/pdf/06_mm6747a6.pdf).

On the other hand, measles is considered to be an infectious disease that can be eliminated because humans are the only natural host of the measles virus, and vaccines with excellent efficacy, safety, and cost are available. Measles elimination is defined as "the absence of endemic measles virus transmission in a defined geographic area, such as a region or country, for 12 months or longer in the presence of a well-performing surveillance system".

In Japan, a two-dose vaccination schedule using the measles-rubella combined (MR) vaccine was introduced in 2006, and at the end of 2007, the "Guidelines for the Prevention of Specific Infectious Diseases: Measles" (hereinafter referred to as the guidelines) were issued. In order to strengthen the immunity against measles among teens, who were the focus of the measles outbreak, a catch-up immunization program for age groups corresponding to the 1st year of junior high school and the 3rd year of high school was implemented for 5 years (from 2008 to 2012) as a routine vaccination. As a result of these countermeasures, the number of measles patients has markedly decreased since 2009, and the Regional Verification Committee of the WHO Western Pacific Region verified in March 2015 that Japan had achieved measles elimination and this status has been maintained as of 2017.

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" (the Infectious Diseases Control Law) (for the notification criteria and disease classification, see: http://www.niid.go.jp/niid/images/iasr/35/410/de4101.pdf). The annual number of notified measles cases was 11,013 in 2008, when measles became a notifiable disease, but the annual number has been 35-732 cases since 2009. In 2018, a total 279 cases of measles were notified (as of February 28, 2019) (Fig. 1). These included an outbreak initiated by a tourist from overseas that reached 101 cases, the largest number of cases since the achievement of measles elimination (see pp. 53 & 54 of this issue), an outbreak initiated by foreign workers (see p. 55 of this issue) and outbreaks that spread through medical facilities (see pp. 57 & 58 of this issue). In addition, an outbreak of measles in a population with low vaccination coverage was reported from January to February 2019 (see p. 60 of this issue).

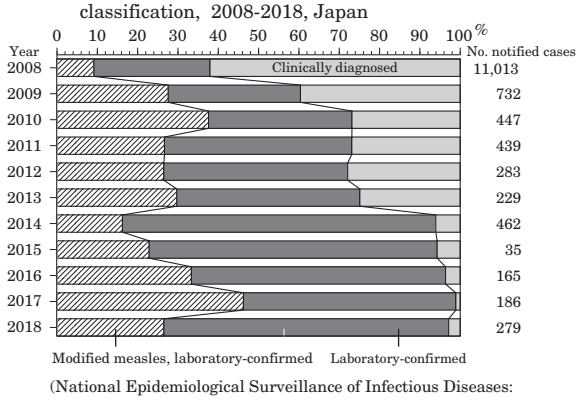
In terms of disease classification the number of measles cases with three main manifestations (fever, rash, and catarrh) was 205 (laboratory-confirmed cases: 197 and clinically-diagnosed cases: 8, 73.5% of the total 279 measles cases) and the number of modified measles cases, which were atypical and laboratory-confirmed with one only or two manifestations, was 74 (26.5% of the total 279 measles case). Since 2016, laboratory-confirmed cases (laboratory-confirmed measles cases and modified measles cases) account for more than 95% of all cases (Fig. 2 in p. 50).

Regarding the age distribution, 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, measles outbreaks occurred mostly among teens and those in their

(Continued on page 50′)

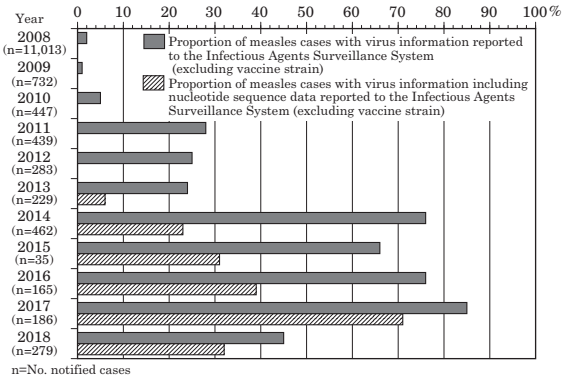
(THE TOPIC OF THIS MONTH-Continued)

Figure 2. Distribution of notified measles cases by disease classification, 2008-2018, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of 28 February 2019)

Figure 4. Reporting status of measles virus information by PHIs to the Infectious Agents Surveillance System, 2008-2018, Japan



(Infectious Agents Surveillance System: as of 28 February 2019)
(National Epidemiological Surveillance of Infectious Diseases: as of 28 February 2019)

twenties, accounting for 65.3% of the measles cases. The number of measles cases in people in their twenties and thirties increased around 2011, and accounted for 65.6% in 2017. In 2018, the proportion of measles cases in people in their twenties and thirties was still high, accounting for 56.7% (Fig. 3 in p. 51).

For cases (n=279) notified in 2018, 63 cases (22.6%) were in non-vaccinated individuals, among which 16 were in infants <1 year of age (25.4% of non-vaccinated individuals) who had not reached the age for routine vaccination. There were 56 cases of (20.1%) 1 dose vaccination, 43 cases (15.4%) of 2 doses vaccination, and the vaccination history was unknown in 117 cases (41.9%) (Table 1 in p. 51).

Two emergency school closures due to measles in 2018 (one each in April and July) were reported by facilities (https://www.niid.go.jp/niid//images/idsc/disease/measles/2018pdf/measschool18_19_03.pdf).

Detection of measles virus (Infectious Agents Surveillance System)

In 2018, there were 146 cases in which the virus genome was detected at prefectural and municipal public health institutes (PHIs), and reported to the Infectious Agents Surveillance System, NESID's laboratory surveillance system, and 125 cases excluding the vaccine strain (44.8% of the total 279 cases). Among these 125 cases, the genotype of the virus was analyzed in 106 cases (38.0% of the total 279 cases), and the nucleotide sequence of the region required for genotyping (450 nucleotides of the N-gene) of the measles virus was also reported in 89 cases (31.9% of the total 279 cases) (excluding the incomplete 4 sequences) (Fig. 4). The breakdown of the reported genotypes of the virus was as follows: 83 cases of genotype D8, 22 cases of genotype B3, 1 case of genotype H1, and 19 cases of unknown type. Among the reported cases with genotype information, 30 were in individuals who had traveled abroad before onset. For individuals with genotype D8 virus, the countries of stay were Thailand (16 cases), Vietnam (4 cases), India, Singapore, and Nepal (1 case for each), and those with genotype B3 virus went to the Philippines (6 cases), the USA and Bangladesh (1 case for each) (including individuals who visited two or more countries) (Table 2 in p. 51).

Current practice regarding laboratory diagnosis

In principle, the guidelines require the implementation of both IgM antibody testing and virus-specific RNA detection testing for all suspected cases of measles. The virus-specific RNA detection test is mainly carried out at PHIs. It is recommended to perform virus genome tests by real-time PCR, and if positive, identify by conventional RT-PCR (nested RT-PCR) to amplify the genotyping site and determine the nucleotide sequence. External quality assessment (EQA) has been conducted to ensure the accuracy of the test at the test laboratory (see p. 61 of this issue).

Vaccination coverage

Since FY2006, 2-dose vaccination using the MR vaccine, the first dose at 1 year of age and the second dose during the year before primary school entry, was introduced into the routine immunization program and is still ongoing. In FY2017, the vaccination coverage was 96.0% for the first dose and 93.4% for the second dose. The vaccine coverage for the first dose exceeded the target of 95% for 8 consecutive years, but the second dose has not reached 95%, although it exceeded 90% for 10 consecutive years (https://www.niid.go.jp/niid/images/idsc/disease/measles/2017-mr-pdf/map5.pdf).

National Epidemiological Surveillance of Vaccine Preventable Diseases (NESVPD)

In FY2018, the NESVPD measles seroprevalence survey was conducted at PHIs in 25 prefectures by measuring the measles gelatin particle agglutination (PA) antibody titer (n=7,268) (see p. 62 of this issue). In principle, the blood collection period ran from July 2018 to September 2018. The proportion of antibodies with a measles PA antibody titer of ≥16 has been ≥95% in all age groups ≥2 since FY2011 (Fig. 5 in p. 51).

Further measures to be taken

Measles is still endemic in many countries (see p. 63 of this issue). In 2018, approximately 31 million people visited Japan from abroad and 19 million Japanese went abroad. With international events, such as the Rugby World Cup, being held in Japan in 2019, the number of overseas visitors is expected to increase. Under such circumstances, it is difficult to completely prevent the entry of the measles virus from abroad. It is important to set up a situation from ordinary times where infection does not spread even if the measles virus is brought in. To this end, it is required to: 1) maintain the vaccination coverage of 2 doses of routine vaccination at 95% or higher and maintain the high antibody positivity level; 2) strengthen surveillance in order for patients to be detected early and appropriate measures to be taken to prevent the further spread of infection; 3) recommend vaccination as necessary to those who have a high risk of infection, including healthcare workers, child welfare facility staff, school officials, overseas travelers, and those who work at places with many opportunities to be in contact with various unspecified people, such as airports (see p. 65 of this issue). In addition, it is also important to promote information sharing among municipalities for smooth epidemiological investigation (see p. 66 of this issue) and to cooperate with global measles controls.

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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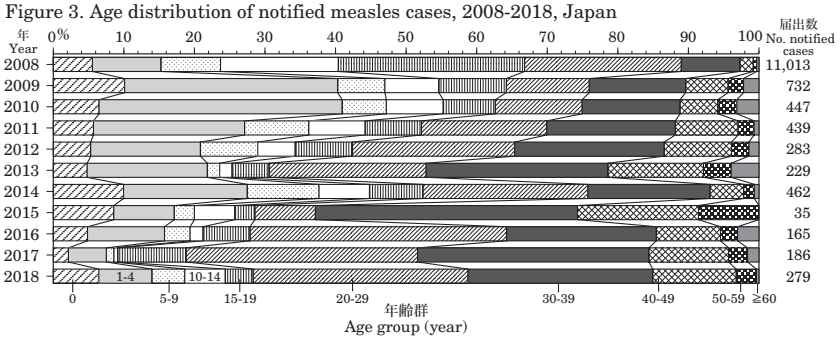
図3. 麻疹患者の年齢分布, 2008～2018年
Figure 3. Age distribution of notified measles cases, 2008-2018, Japan



(感染症発生動向調査：2019年2月28日現在届出数)
(National Epidemiological Surveillance of Infectious Diseases: as of 28 February 2019)

表1. 麻疹患者の予防接種歴別届出数, 2008～2018年
Table 1. Yearly number of notified measles cases by vaccination status, 2008-2018, Japan

年 Year	接種歴なし Not vaccinated	1回接種 1 dose of MCV**	2回接種 2 doses of MCV**	接種歴不明 Unknown	患者届出数 No. notified 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)	46 (1)	21	86	186 (4)
2018	63 (16)	56 (2)	43	117	279 (18)

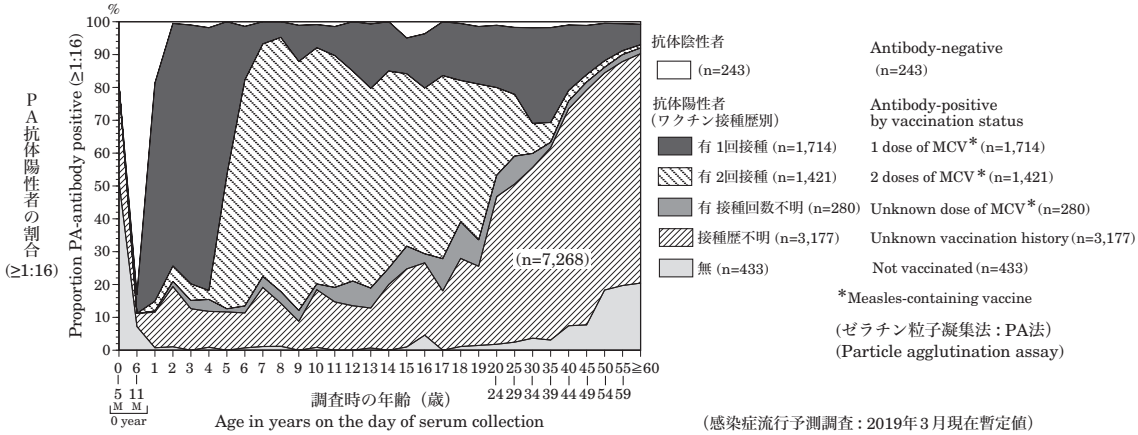
*うち( )は0歳　(感染症発生動向調査：2019年2月28日現在届出数)
*No. notified cases < 1 year of age indicated in parenthesis　**Measles-containing vaccine
(National Epidemiological Surveillance of Infectious Diseases: as of 28 February 2019)

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, 2018年
Table 2. Measles virus isolation/detection by epidemiological situation, travel history and destination abroad, 2018

遺伝子型 Genotype	例数 No. of cases	発生の状況† Epidemiological situation†				渡航歴 無／不明 No/unknown travel history	渡航歴 有 Travel history abroad	渡航先* Destination abroad*							
		散発 Sporadic	家族内発生 Familial	地域流行 Local	集団発生 Outbreak			米国 USA	フィリピン Phillipine	バングラデシュ Bangladesh	インド India	シンガポール Singapore	タイ* Thailand*	ネパール Nepal	ベトナム* Vietnam*
合計 Total	125	80	10	18	18	95	30	1	6	1	1	1	16	1	4
Not typed	19	12	1	2	4	19	–	–	–	–	–	–	–	–	–
B3	22	9	1	1	11	14	8	1	6	1	–	–	–	–	–
D8	83	58	8	15	3	61	22	–	–	–	1	1	16	1	4
H1	1	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：2019年2月28日現在報告数)
†Including multiple situations　*Including those who has visited two or more countries (e.g. Thailand/Vietnam)
[Infectious Agents Surveillance System: as of 28 February 2019 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, 2018年度
Figure 5. Proportion of seropositive against measles virus by age and vaccination status, fiscal year 2018, Japan



(感染症流行予測調査：2019年3月現在暫定値)
(National Epidemiological Surveillance of Vaccine-Preventable Diseases: as of March, 2019)