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

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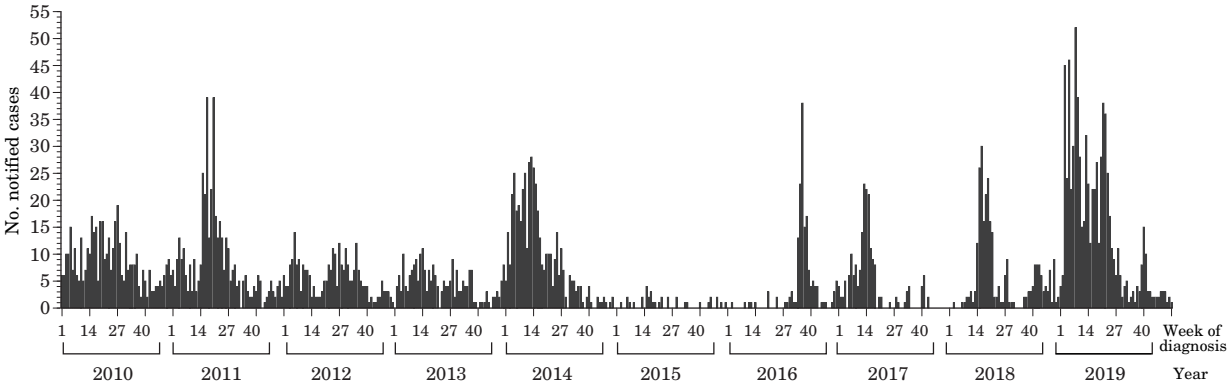
<THE TOPIC OF THIS MONTH>
Measles in Japan, as of February 2020

Figure 1. Weekly number of notified measles cases, 2010-2019, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of 27 February 2020)

Measles is an acute viral disease caused by the measles virus, characterized by fever, rash, and catarrh. The measles virus is transmitted by aerosol, droplets, or contact infection, and is highly contagious. The incubation period is 10-12 days, and the infectious period of the virus is from 1 day before onset to 3 days after the fever has subsided. There are few subclinical infections. Before the introduction of the measles vaccine (before 1965), most people were infected by the age of 15. However, due to the improvement of vaccination coverage, the number of measles cases has decreased and been ranging from tens to hundreds in recent years. In addition, many patients are over 20 years old.

As the measles virus infects immune cells, the host becomes acutely immunocompromised, resulting in complications such as otitis media, enteritis, encephalitis, and pneumonia. Those who develop pneumonia and encephalitis may die. It has also been reported that the measles virus damages the host's immune memory cells, impairing immunity to other infectious diseases acquired in the past, and making the host more susceptible to reinfection with those infectious diseases. Although it is rare, patients may develop encephalitis with a poor prognosis known as subacute sclerosing panencephalitis (SSPE). In addition, measles infection during pregnancy can cause stillbirth or miscarriage. The World Health Organization (WHO) estimates that more than 140,000 persons, mainly children in developing countries, died from measles in 2018 (https://www.who.int/news-room/detail/05-12-2019-more-than-140-000-die-from-measles-as-cases-surge-worldwide).

On the other hand, measles is considered to be an infectious disease that can be eliminated because there is an excellent live attenuated vaccine. In 2005, the WHO Western Pacific Region (WPR), to which Japan belongs, resolved to eliminate measles from the region by 2012. In response to this, in Japan, a two-dose measles vaccination schedule (the 1st dose: 1-year-old children, the 2nd dose: children during the year before elementary school entry) was introduced in 2006 instead of a single-dose vaccination schedule. However, due to the outbreak of measles among teens in 2007, the Ministry of Health, Labour and Welfare (MHLW) issued the "Guidelines for the Prevention of Specific Infectious Diseases: Measles" (hereinafter referred to as the guidelines) at the end of 2007 and took countermeasures, including implementation of the catch-up immunization program for age groups corresponding to the 1st year of junior high school (3rd dose) and the 3rd year of high school (4th dose) for 5 years (from 2008 to 2012) as a routine vaccination in order to boost the immunity against measles among teens who had no opportunity for a second dose of the measles vaccine. As a result, the number of measles patients has decreased since 2009, and the Regional Verification Committee of the WHO WPR verified in March 2015 that Japan had eliminated measles and this status has been maintained to date.

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" (referred to as 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 in Japan was 11,013 in 2008 when measles became a notifiable disease, but it has markedly decreased since 2009.

In 2019, 745 cases of measles, the highest number of cases since 2009, were notified (Fig. 1). They included outbreaks, such as an outbreak in an organization that emphasizes life independent of medicine, including vaccines, which spread to 8 prefectures with 74 cases (see p. 56 of this issue), and an outbreak that spread mainly in large commercial facilities (see p.57 of this issue). An emergency school closure due to measles (week 22) was reported to the measles outbreak investigation by the facility (https://www.niid.go.jp/niid//images/idsc/disease/measles/2019pdf/measschool19_20_03.pdf).

(Continued on page 54′)

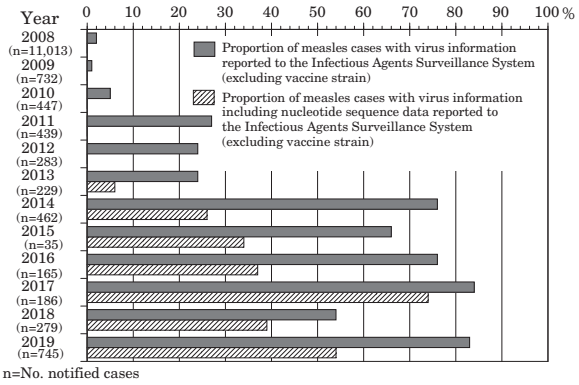
(THE TOPIC OF THIS MONTH-Continued)

In terms of disease classification, 539 cases (laboratory-confirmed cases: 520 and clinically-diagnosed cases: 19, 72.3% of the total 745 measles cases) had all three main symptoms of measles (fever, rash, and catarrh), and the number of modified measles cases that were atypical with only one or two manifestation and laboratory-confirmed, was 206 (27.7% of the total 745 measles cases).

Regarding the age distribution, patients over 20 years old accounted for 70.2% of all patients (523 / 745) (Fig. 2 in p.55).

Among the cases notified in 2019 (n=745), 195 (26.2%) were in unvaccinated individuals, among whom 36 were infants <1 of age (18.5% of unvaccinated individuals) who had not reached the age for routine vaccination. There were 161 (21.6%) who received one dose, 104 (14.0%) who received two doses, and 285 (38.3%) with unknown vaccination history (Table 1 in p.55).

Figure 3. Reporting status of measles virus information by PHIs to the Infectious Agents Surveillance System, 2008-2019, Japan



(Infectious Agents Surveillance System: as of 17 February 2020)
(National Epidemiological Surveillance of Infectious Diseases: as of 27 February 2020)

Current practice regarding laboratory diagnosis

In principle, the guidelines revised in 2012 require the implementation of both IgM antibody test and virus-specific RNA detection test (real-time RT-PCR) for all clinically-diagnosed measles cases. The IgM antibody tests are conducted at private laboratories, and the virus-specific RNA detection tests are mainly carried out at the Prefecture and Municipal Public Health Institutes (PHIs). In 2019, 726 (97.4%) of 745 measles cases were notified as laboratory-confirmed cases. In order to demonstrate that Japan has maintained the measles elimination status, it is necessary to confirm the absence of endemic measles virus transmission for more than 12 months in Japan. Nucleotide sequence analysis of the region for genotyping of the measles virus (450 nucleotides) is required to confirm the links in outbreaks and to distinguish whether the cases are imported.

Detection of measles virus (Infectious Agents Surveillance System)

In 2019, there were 640 cases, 616 excluding the vaccine strains (82.7% of the total 745 cases), in which the virus genome was detected at PHIs and reported to the Infectious Agents Surveillance System, NESID's laboratory surveillance system. Among these 616 cases, the genotype of the virus was analyzed in 576 (77.3% of the total 745 cases), and the nucleotide sequence of the region required for genotyping (450 nucleotides) of the measles virus was also reported in 400 cases (53.7% of the total 745 cases) (including reports by the accession number of the gene banks and excluding the incomplete 7 sequences) (Fig. 3). The breakdown of the reported genotype of the virus was as follows: 402 cases of genotype D8, 174 cases of genotype B3, and 40 cases of "not typed." Among the reported cases with genotype information, 107 were in individuals who had traveled abroad before onset. For individuals with genotype D8 viruses (65 cases in total), the countries of stay were Vietnam (29 cases), Thailand (14 cases), Myanmar (5 cases), Republic of Maldives (5 cases), etc., and those with genotype B3 viruses (38 cases in total) went to the Philippines (31 cases), Hong Kong (4 cases), China (2 cases), etc. (including cases who visited two or more countries) (Table 2 in p.55).

Vaccination coverage

Since fiscal year (FY) 2006, 2-dose vaccination (the 1st dose and the 2nd dose) using the MR vaccine was introduced into the routine immunization program and is still ongoing. In FY2018, the vaccination coverage was the highest ever, with 98.5% for the 1st dose and 94.6% for the 2nd dose. The coverage of the 1st dose exceeded the target of 95% not only overall (for 9 consecutive years), but also in each prefecture. The coverage for the 2nd dose exceeded 90% for 11 consecutive years, but was slightly short of 95% (https://www.niid.go.jp/niid/images/idsc/disease/measles/2018-mr-pdf/2018_0-1_1.pdf).

National Epidemiological Surveillance of Vaccine Preventable Diseases (NESVPD)

In FY2019, the NESVPD measles seroprevalence survey was conducted at the PHIs in 24 prefectures by measuring the measles gelatin particle agglutination (PA) antibody titer (n=6,628) (see p. 58 of this issue). In principle, the blood collection period ran from July 2019 to September 2019. The proportion of antibodies with a measles PA antibody titer of ≥16 has been ≥95% for all age groups ≥2 years since FY2014 (Fig. 4 in p.55).

Further measures to be taken

Measles is a highly contagious disease with marked mortality. Although many measures towards measles elimination have been implemented worldwide, it is still epidemic in many countries (see p. 59 of this issue). Now that traffic between Japan and overseas is frequent, and it is difficult to prevent the entry of the measles virus from abroad, it is essential to prepare an environment in which infection does not spread even if brought in. To this end, the following are required: 1) maintain the vaccination coverage of 2 doses of routine vaccination at 95% or higher and maintain a high antibody positivity level among the general population: 2) further strengthen surveillance in order for patients to be detected early and appropriate measures can 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 opportunities to be in contact with unspecified people such as airports. Moreover, it is necessary to collaborate with international organizations to provide international cooperation to countries with an insufficient medical environment (see p. 61 of this issue). In addition, it is also important to offer education and reliable information to promote the understanding of the benefits of vaccines in response to reluctance or refusal to receive available vaccines (referred to as "vaccine hesitancy"), one of the public health threats listed by WHO in 2019.

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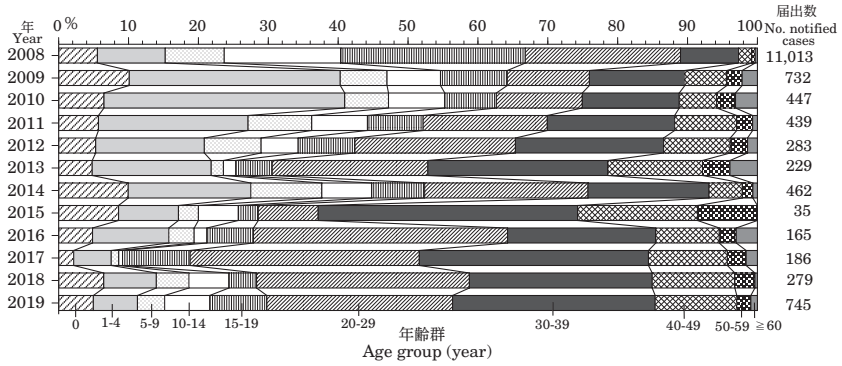
（特集つづき）（THE TOPIC OF THIS MONTH-Continued）

図2. 麻疹患者の年齢分布，2008～2019年
Figure 2. Age distribution of notified measles cases, 2008-2019, Japan



（感染症発生動向調査：2020年2月27日現在届出数）
(National Epidemiological Surveillance of Infectious Diseases: as of 27 February 2020)

表1. 麻疹患者の予防接種歴別届出数, 2008～2019年
Table 1. Yearly number of notified measles cases by vaccination status, 2008-2019, 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)
2019	195 (36)	161 (1)	104	285	745 (37)

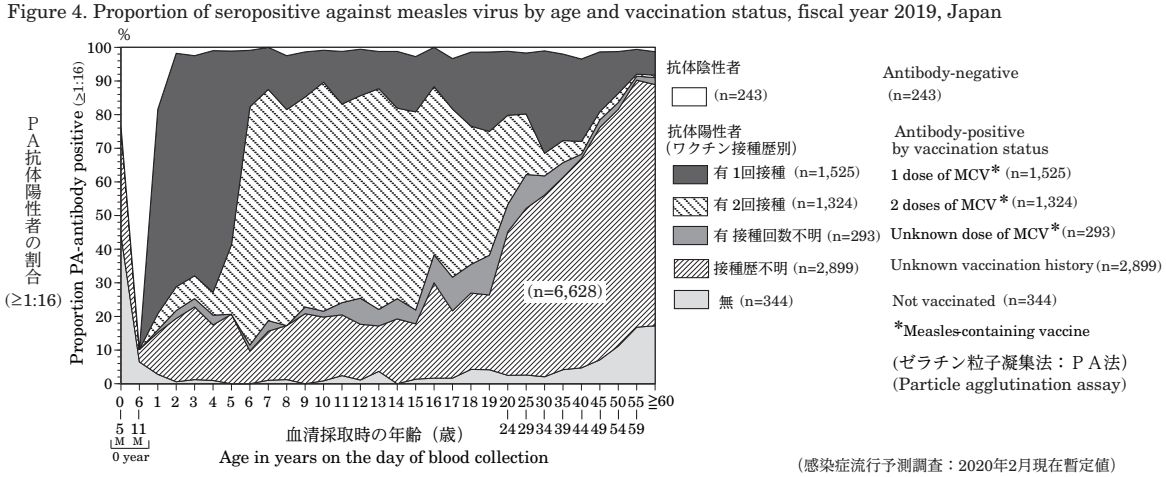
（ ）内は0歳再掲 （感染症発生動向調査：2020年2月27日現在届出数）
No. notified cases < 1 year of age indicated in parenthesis *Measles-containing vaccine
(National Epidemiological Surveillance of Infectious Diseases: as of 27 February 2020)

Table 2. Measles virus isolation / detection by epidemiological situation, travel history and destination abroad, 2019

Genotype	No. of cases	Epidemiological situation †				No/unknown travel history	Travel history abroad	Destination abroad*																								
		Sporadic	Familial	Local	Outbreak			Myanmar	Italy	Malaysia	Korea	Cambodia	Philippines	Bangladesh	Brazil	Canada	Turkey	Ukraine	Singapore	Germany	UK	USA	Sri Lanka	New Caledonia	Laos*	Qatar*	Nepal*	India*	China*	Thailand*	Hong Kong*	Maldives*	Vietnam*
Total	616	408	65	13	136	509	107	6	1	2	1	2	32	1	1	1	1	2	1	1	1	1	2	1	1	1	1	1	3	15	5	5	29
not typed	40	32	1	-	7	36	4	1	-	-	-	-	1	-	-	-	-	-	-	-	-	1	-	-	-	1	1	1	-	1	-	-	-
B3	174	137	13	1	24	136	38	-	-	-	-	-	31	1	-	-	1	-	-	-	1	-	-	-	-	-	-	-	2	-	4	-	-
D8	402	239	51	12	105	337	65	5	1	2	1	2	-	-	1	1	-	2	1	1	-	-	2	1	1	-	-	-	1	14	1	5	29

† Including multiple situations. *Including cases who has visited two or more countries (e.g. Thailand / Vietnam)
[Infectious Agents Surveillance System: as of 28 February 2020 from prefectural and municipal public health institutes (PHIs)]

図4. 年齢別／年齢群別麻疹抗体保有状況，2019年度
Figure 4. Proportion of seropositive against measles virus by age and vaccination status, fiscal year 2019, Japan



（感染症流行予測調査：2020年2月現在暫定値）
(National Epidemiological Surveillance of Vaccine-Preventable Diseases: as of February, 2020)