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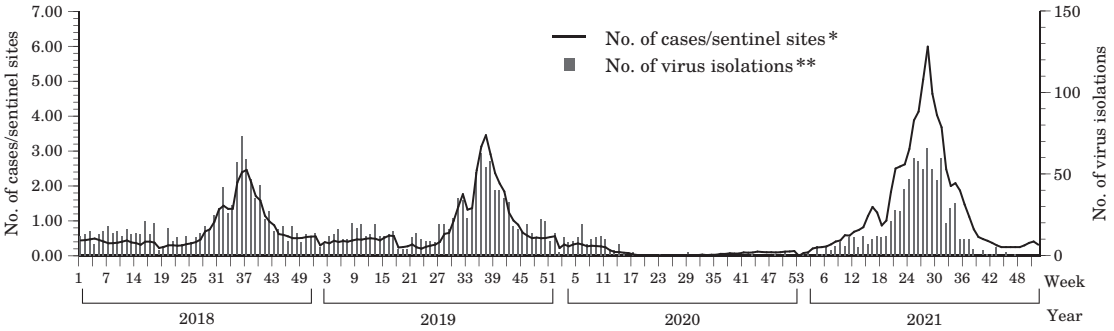
National Institute of Infectious Diseases and Tuberculosis and Infectious Diseases Control Division, Ministry of Health, Labour and Welfare

<THE TOPIC OF THIS MONTH>
Respiratory syncytial virus infection, 2018-2021, Japan

Figure 1. Weekly number of reported RS virus infection cases per sentinel sites and RS virus isolations, week 1 of 2018 to week 52 of 2021, Japan



*National Epidemiological Surveillance of Infectious Diseases/pediatric sentinel sites: as at 19 January 2022
**Infectious Agents Surveillance System: as at 28 February 2022

Respiratory syncytial virus (RSV) belongs to the family *Pneumoviridae*, genus *orthopneumovirus*. The virus was formerly named RSV as a virus belonging to the family *Paramxyoviridae*, subfamily *Pneumovirinae*, genus *pneumovirus*, but currently, its official nomenclature is human orthopneumovirus, and RSV is its common name. RSV is broadly divided into two subgroups (subgroups A and B) depending on the character of the attachment glycoprotein (G protein) and further divided into several genotypes based on the G protein sequence (see pp. 82 and 84 of this issue). RSV is present globally and almost everyone experiences infection during childhood. RSV induces various clinical manifestations from mild flu-like illness to lower respiratory tract infection; in particular, infants under 6 months of age tend to have severe disease (see p. 85 of this issue). In addition, RSV easily re-infects adults, and severe infections in the elderly have become a public health concern in developed countries in recent years (see p. 87 of this issue). In Japan, symptomatic RSV infection is classified as a Category V Infectious Disease under the Infectious Diseases Control Law, monitored via pediatric sentinel sites; the designated notification sites (approximately 3,000 sentinel pediatric medical facilities) must report to the Public Health Center every week. Laboratory diagnosis is mandatory for notification (https://www.mhlw.go.jp/bunya/kenkou/kekkaku-kansenshou11/01-05-15.html).

Epidemiologic situation of RSV infections

The number of reported RSV infection cases per sentinel site started to increase from week 27 (July) in both 2018 and 2019, peaked at week 37 (September) (2018, 2.46 reports/sentinel; 2019, 3.45 reports/sentinel), and decreased toward the end of the year. In 2020, although the number of reported cases per sentinel site was similar to previous years through around week 15 (April), it shifted to a lower level from May to August. The number of reported cases increased in September, but there was no remarkable epidemic throughout the year. In 2021, the increasing trend from the previous year continued, and the number peaked at week 28 in July (5.99/per sentinel site). The respective number of reported cases per sentinel site and the total number of reported cases for each year were as follows: 2018, 38.29 and 120,743; 2019, 44.39 and 140,093; 2020, 5.74 and 18,097; 2021, 71.96 and 226,823 (Fig. 1).

Since 2014, RSV infections have tended to start in Okinawa Prefecture in the summer and then spread throughout Japan (IASR 35: 137-139, 2014). Although the epidemic peaked at the end of the calendar year through 2015, it began earlier from 2016 and peaked in September in 2017. In both 2018 and 2019, an epidemic was observed in Okinawa Prefecture in the summer, followed by a nationwide epidemic with a peak in September. In 2020, the number of reports began to increase in Okinawa and Kagoshima Prefectures from September, and from 2021, the trend continued to increase, mostly in the Kyushu and Kinki regions, through around March 2021. The epidemic subsequently spread nationwide, peaking in July. After a temporary decline, the epidemic increased from September in Kagoshima Prefecture and from October in Okinawa Prefecture to the end of the year (Fig. 2 on p. 80).

Regarding the age distribution of patients with RSV infection from 2018 to 2021, reports of patients aged 2 years or younger accounted for about 85% (2018, 88.6%; 2019, 86.8%; 2020, 85.0%) during the 3 years from 2018 to 2020, with the most frequent report

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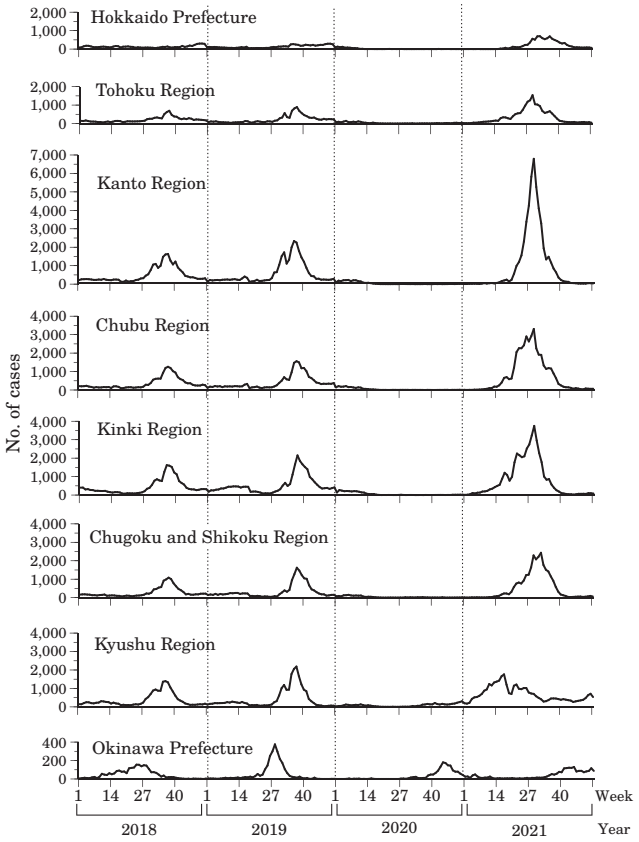
(THE TOPIC OF THIS MONTH-Continued)

by age group being one-year-olds, followed by zero- and then two-year-olds. In 2021, the number of reports for children aged 2 years or younger decreased to about 74%, and the order by age was one-year-olds (30.3%), two-year-olds (24.4%), and zero-year-olds (18.9%). In addition, the proportion of those aged 3–9 years in 2021 was 26.1%, higher than that of the three years from 2018 to 2020 (2018, 11.1%; 2019, 12.9%; 2020, 14.3%). The proportion of male patients was slightly higher throughout the observation period (54.2% in 2018, 53.4% in 2019, 53.1% in 2020, and 52.5% in 2021) (Fig. 3 on p. 81).

Figure 2. Weekly number of reported RS virus infection cases by region, week 1 of 2018 to week 52 of 2021, Japan



(National Epidemiological Surveillance of Infectious Diseases/pediatric sentinel sites: as at 19 January 2022)

Detection of RSV and other respiratory viruses

As at February 28, 2022, respiratory viruses detected from samples collected between 2018 and 2021 at Public Health Institutes and reported to the Infectious Agents Surveillance System (IASS), National Epidemiological Surveillance of Infectious Diseases (NESID), included influenza virus, rhinovirus, RSV, parainfluenza virus, human metapneumovirus, human bocavirus, human coronaviruses, and SARS-CoV-2 (Table on p. 81) (see p. 88 of this issue). In 2018 and 2019, detections of influenza virus were the most frequent (2018, 9,140; 2019, 10,229), accounting for nearly 70% of the total reported detections, while in 2020 and 2021, SARS-CoV-2 was the most frequently detected owing to the COVID-19 pandemic. On the other hand, in 2020 and 2021, detections of influenza virus decreased substantially from 2,730 (12.8%) in 2020 to 6 (0.03%) in 2021, probably because there was no circulation of influenza. Although the distribution of detected viruses varied depending on the year, the number of RSV (rank based on number of detections) was 1,030 (3rd) in 2018, 1,029 (3rd) in 2019, 132 (6th) in 2020, and 841 (2nd) in 2021. Because the reporting process may take time in IASS, the presented number of cases detected in 2021 may be lower than the actual number (Table and Fig. 4 on p. 81). Temporal detections of RSV correlated with the epidemic situation of RSV infection occurrence, and the number of detections increased from June to December in 2018 and 2019, and from March to September in 2021 (Fig. 1 on p. 79). Among the 3,032 cases of RSV detection, the most commonly used method was gene detection (2,906 cases, 95.8%) and the most frequently used specimen was pharyngeal swab (2,969 cases, 97.9%). Among the patients with RSV detection, 2,623 (86.5%) showed symptoms associated with upper or lower respiratory tract infection, and 263 (8.7%) had also developed pneumonia. In addition, 22 cases (0.7%) were detected from patients with encephalitis/encephalopathy, indicative of severe infection.

Vaccine development and global surveillance for RSV

In 2015, the World Health Organization (WHO) started discussions on the RSV global surveillance system, which utilizes the pre-existing Global Influenza Surveillance and Response System (GISRS) platform (see pp. 90 and 92 of this issue). The background context was that the maternal vaccine developed by Novavax Inc. was to be approved around 2018, and there was an urgent need to establish an RSV surveillance system. The first phase of pilot surveillance started in 2016 and the second in 2019; however, Novavax's vaccine has not yet been approved, and pilot surveillance has not progressed due to the COVID-19 pandemic. On the other hand, many new formulations have been approved as COVID-19 vaccines, which has helped accelerate the development of RSV vaccines (see p. 94 of this issue).

Issues for the future

Because RSV often causes severe infection in infants and the elderly, it is important to monitor its epidemics. However, since RSV surveillance in Japan is based only on reports from pediatric sentinel sites, it is difficult to understand the epidemiology of RSV infections in patients other than children. In addition, because there are no surveillance data that apply syndromes/symptoms as the denominator, it is difficult to calculate the disease burden. It is necessary to understand the disease burden in all age groups and evaluate preventive measures. In addition, it is also essential to discuss how to participate in RSV global surveillance, promoted by WHO with the purpose of RSV vaccine and drug development.

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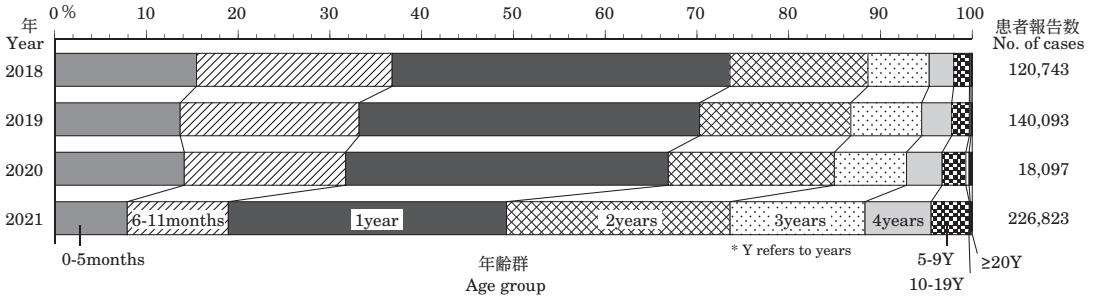
(特集つづき) (THE TOPIC OF THIS MONTH-Continued)

図3. RSウイルス感染症患者の年齢分布, 2018～2021年
Figure 3. Age distribution of reported RSV infection cases, 2018-2021, Japan



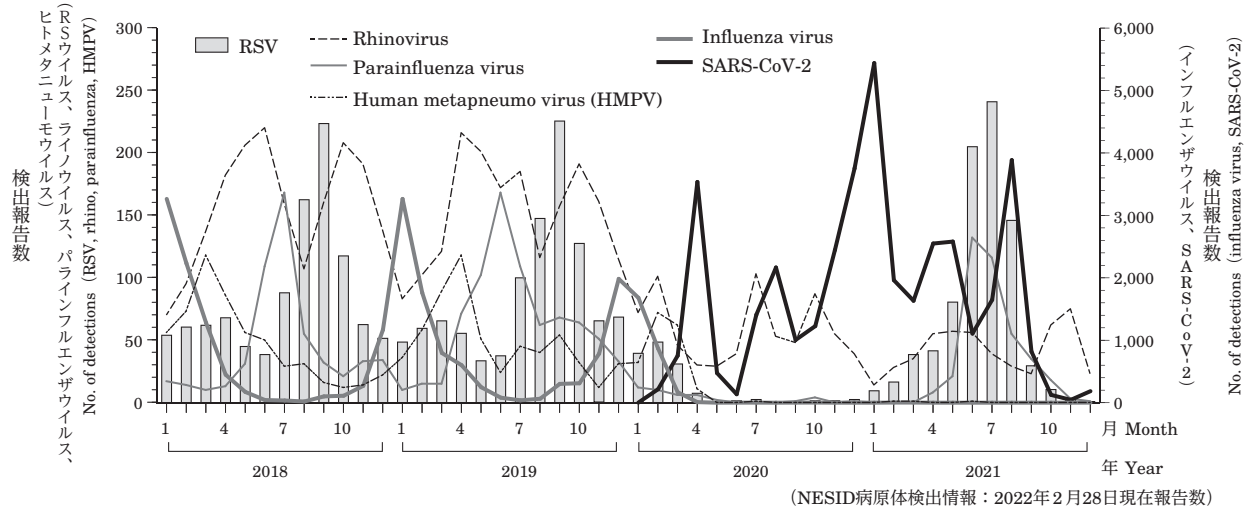
(感染症発生動向調査・小児科定点：2022年1月19日現在報告数)
(National Epidemiological Surveillance of Infectious Diseases/Pediatric Sentinel Sites: as at 19 January 2022)

表. 検体採取年別呼吸器系ウイルス検出状況, 2018～2021年
Table. Reported number of isolations/detections of respiratory viruses during 2018-2021, Japan

検出ウイルス Virus	検体採取年 Sampling year				
	2018	2019	2020	2021	Total
Respiratory syncytial virus (RSV)	1,030	1,029	132	841	3,032
Rhinovirus	1,873	1,820	702	496	4,891
Parainfluenza virus	537	768	42	389	1,736
Parainfluenza virus 1	138	134	30	22	324
Parainfluenza virus 2	24	186	5	4	219
Parainfluenza virus 3	333	402	1	343	1,079
Parainfluenza virus 4	41	46	6	20	113
Parainfluenza virus not typed	1	0	0	0	1
Human metapneumovirus	563	590	191	3	1,347
Human bocavirus	128	123	59	71	381
Human coronavirus	173	164	281	156	774
Human coronavirus 229E	26	1	69	0	96
Human coronavirus HKU1	24	34	63	8	129
Human coronavirus NL63	68	67	18	77	230
Human coronavirus OC43	54	62	131	71	318
Human coronavirus not typed	1	0	0	0	1
SARS-CoV-2	−	−	17,119	21,975	39,094
Influenza virus A not subtyped	14	16	3	0	33
Influenza virus A H1pdm09	1,989	5,194	1,997	0	9,180
Influenza virus A H3	3,355	4,286	42	6	7,689
Influenza virus B	3,727	725	674	0	5,126
Influenza virus C	55	8	14	0	77
Total	13,444	14,723	21,256	23,937	73,360

− : not applicable
(NESID病原体検出情報：2022年2月28日現在報告数)
[Infectious Agents Surveillance System: as at 28 February 2022 from prefectural and municipal public health institutes (PHIs)]

図4. 検体採取月別呼吸器系ウイルス (RSウイルス、ライノウイルス、パラインフルエンザウイルス、ヒトメタニューモウイルス、インフルエンザウイルス、SARS-CoV-2)、検出状況, 2018～2021年
Figure 4. Number of respiratory viruses detected/isolated from clinical specimens, by month of sample collection, 2018-2021, Japan



(NESID病原体検出情報：2022年2月28日現在報告数)
[Infectious Agents Surveillance System: as at 28 February 2022 from prefectural and municipal public health institutes (PHIs)]