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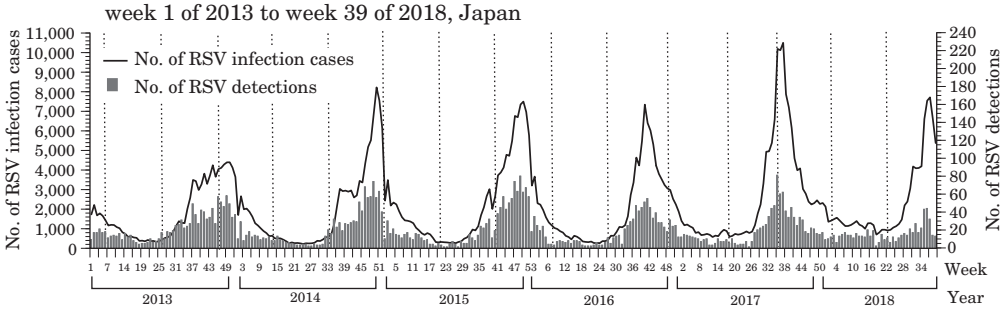
National Institute of Infectious Diseases and
Tuberculosis and Infectious Diseases
Control Division,
Ministry of Health, Labour and Welfare

<THE TOPIC OF THIS MONTH>
Respiratory syncytial virus infection, January 2014-September 2018

Figure 1. Weekly number of reported RSV infection cases* and RSV detections**, week 1 of 2013 to week 39 of 2018, Japan



* National Epidemiological Surveillance of Infectious Diseases: as of 31 October 2018
** Infectious Agents Surveillance System: as of 5 November 2018

Respiratory syncytial virus (RSV) is an RNA virus belonging to the family *Pneumoviridae* (see p. 213 of this issue). *Pneumoviridae* is composed of the genus Metapneumovirus, which includes human metapneumovirus (see p. 217 of this issue), and the genus Orthopneumovirus, which includes RSV. Based on phylogenetic analysis of the nucleotide sequence of the G gene, RSV is classified into two subgroups, RSV-A and RSV-B (see pp. 213 and 215 of this issue). RSV is transmitted via droplets or contact. Although at least 50% of infants become infected during their first year of life and nearly 100% by their second year, life-long immunity is not achieved. In infants, approximately 50% of pneumonia and 50-90% of bronchiolitis are due to RSV.

Newborns, infants, and the immunocompromised are at risk of severe outcomes from RSV infection. Complications include apnea and acute encephalopathy. Among adults, RSV infection often manifests as cold-like symptoms, but there is an increase in severity for the elderly with underlying conditions such as chronic respiratory disease. Preventing transmission from infected children or adults to the elderly is also important (see p. 212 of this issue). With an outbreak reported at a facility caring for immune-deficient patients with blood disorders, infection control measures are considered to be important (see p. 211 of this issue).

For RSV infection, treatment is supportive such as oxygen administration, infusion therapy, or respiratory management. In addition, to prevent severe outcomes from RSV infection for high-risk groups (e.g. preterm infants and those of young age with bronchopulmonary dysplasia or with congenital heart disease), the use of palivizumab, a humanized monoclonal antibody against RSV F glycoprotein, is covered by national health insurance. Although palivizumab administration has been reported to be effective for preventing severe outcomes from RSV infection, appropriate planning for its use is important, as the level of RSV in circulation and the individuals targeted for treatment need to be considered (see p. 219 of this issue). Development of an RSV vaccine is in progress, and in recent years, the World Health Organization has been actively discussing RSV vaccine development and future implementation, along with global surveillance of RSV (see p. 220 of this issue).

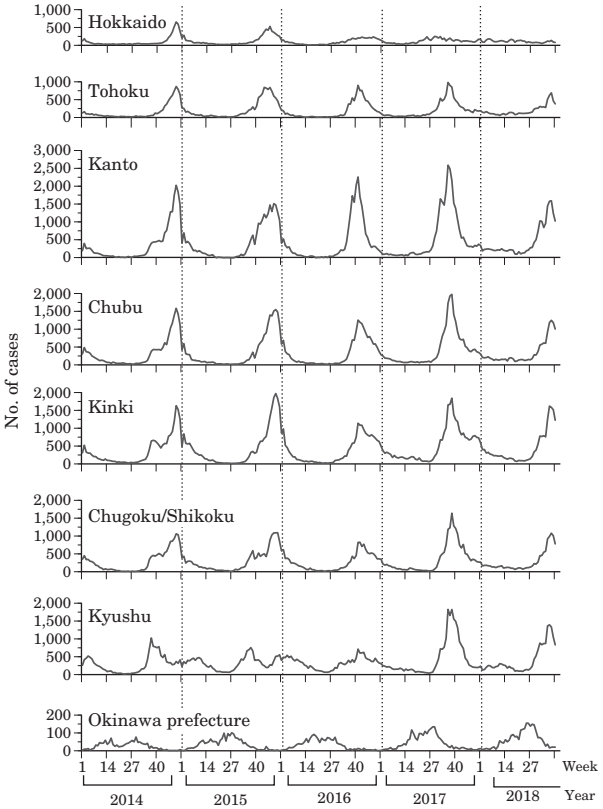
In accordance with the amendment of the Infectious Diseases Control Law (effective November 5, 2003), RSV infection was added to the list of category V infectious diseases; it is monitored under the National Epidemiological Surveillance of Infectious Diseases (NESID) Program's pediatric sentinel surveillance system, and reporting requires laboratory diagnosis (http://www.niid.go.jp/niid/images/iasr/35/412/de4121.pdf). Since October 17, 2011, the use of the RSV antigen detection test has been covered by national health insurance for infant outpatients or outpatients for whom palivizumab is indicated, expanding beyond inpatient use (until March 31, 2006, coverage was limited to hospitalized patients under 3 years of age; after this date, it was expanded to inpatients of any age). The number of pediatric sentinel sites, particularly clinics, reporting RSV infection has been increasing yearly (https://www.niid.go.jp/niid/images/iasr/35/412/graph/f4121.gif), and when interpreting the RSV infection notification trends, it is necessary to consider aspects such as the expansion of the health insurance coverage for laboratory diagnosis (see p. 210 of this issue). As ~80% of the pediatric sentinel sites reported RSV infection in recent years, RSV infection has been presented as the number of reported cases per sentinel since week 9 of 2018, the same format as the other infectious diseases monitored under the pediatric sentinel surveillance system.

(Continued on page 208′)

(THE TOPIC OF THIS MONTH-Continued)

RSV infections based on NESID: In 2017, notifications of RSV infection began to increase continuously from July, prior to seasonal influenza, peaking in September. Through 2015, notifications increased in the fall with a peak late in the calendar year. However, since 2016, notifications have begun to increase earlier, with the peak observed in the fall (the peak week was week 40 in 2016, week 37 in 2017, and albeit provisional, week 37 in 2018) (Fig. 1 in p. 207). In addition, in 2017 and 2018, there were more notifications during the summer than in previous years. Historically, RSV infection has been known to show seasonality characteristic for the region (IASR 35: 137-139, 2014), and Okinawa prefecture continued to show a peak during the summer also after 2014, whereas the Kyushu region had an earlier peak than other regions through 2015. However, in 2017, the peak week recorded for the Kanto and Tohoku regions was week 35, the same as that for Kyushu, and no clear peak was observed for Hokkaido (Fig. 2). The sex and age distributions of the reported cases in 2017 were similar to those reported in the previous update (IASR 35: 137-139, 2014), with a slight male predominance [74,555 males (53%) and 64,891 females (47%)] and the majority aged ≤ two years (88%). However, although notifications were previously greatest among those under one year of age, followed by one-year-olds and two-year-olds (IASR 35: 137-139, 2014), the distribution changed in 2017, the year with the largest number of notifications reported since surveillance for RSV infection began in 2003; one-year-olds were the most numerous, followed by those under one year of age and two-year-olds (Fig. 3 in p. 209).

Figure 2. Weekly number of reported RSV infection cases by region, week 1 of 2014 to week 39 of 2018, Japan



(National Epidemiological Surveillance of Infectious Diseases: as of 31 October 2018)

During January 2014 to September 2018, among the 2,951 patients reported as acute encephalitis, a category V infectious disease requiring notification, 41 were recorded with RSV as the causative agent (provisional data as of October 31, 2018); 21 were male and 20 were female, and the median age was one year (range: 1-6 years), with 33 aged 0-2 years, the age at which RSV infection tends to be severe (Table 1 in p. 209).

Detection of RSV and other respiratory viruses: Prefectural and municipal public health institutes (PHIs) test for pathogenic agents from specimens collected predominantly at sentinel sites designated for laboratory-based surveillance [composed of approximately 10% of the ~5,000 influenza sentinel sites (including the ~3,000 pediatric sentinel sites) and ~500 sentinel hospitals distributed across the country]. During the 2013/14 season (based on the influenza season from September to August in the following year) to the 2017/18 season, the frequency of viruses isolated/detected in the order of highest to lowest was influenza virus, rhinovirus, RSV, parainfluenza virus, and human metapneumovirus (see p. 217 of this issue) (Table 2 in p. 209). The viruses isolated/detected differed based on the time of the year at which the specimens were collected, and although variable by year, RSV tended to be frequent from September to December and influenza virus from December to March, similar to the trends noted in the sentinel patient-based surveillance data. Regarding human metapneumovirus, it was found most frequently from February to May (Fig. 4 in p. 209).

During the 2013/14 to the 2017/18 seasons, RSV detections from 5,324 persons were reported from 60 PHIs located across the country (as of November 13, 2018). Throat swabs comprised the majority of the RSV-positive specimens (5,258 specimens, 99%). The most frequent detection method was gene detection (n=5,177, 97%), followed by cell culture isolation (n=590, 11%) and antigen detection (n=23, <1%) (includes detection by more than one method). The most frequent diagnosis recorded at the time of specimen collection was "RSV infection associated with respiratory tract infection" (n=2,392, 45%), followed by "lower respiratory tract inflammation" (n=1,758, 33%) and "upper respiratory tract inflammation" (n=460, 9%), comprising ~90% of all the diagnoses.

Summary and challenges: In recent years, the number of sentinel sites reporting RSV infection has stabilized, and information has been fed back as the number of cases per sentinel site since week 9 of 2018. On the other hand, as denominator information based on clinical syndrome or symptoms is unavailable in Japan, interpretation of trends require caution (see p. 210 of this issue). In addition, estimating disease burden is a challenge (see p. 220 of this issue). Although RSV infection is of concern for the elderly (see p. 212 of this issue) and high-risk individuals, the current surveillance system is limited to reports from pediatric sentinel sites, and understanding the epidemiology of RSV infection in non-pediatric populations is difficult. In the future, it will be important to consider assessing RSV infection's disease burden and the necessary measures for all age groups.

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, 2014～2017年

(感染症発生動向調査・小児科定点 : 2018年10月31日現在報告数)

Figure 3. Age distribution of reported RSV infection cases, 2014-2017, Japan

(National Epidemiological Surveillance of Infectious Diseases: as of 31 October 2018)

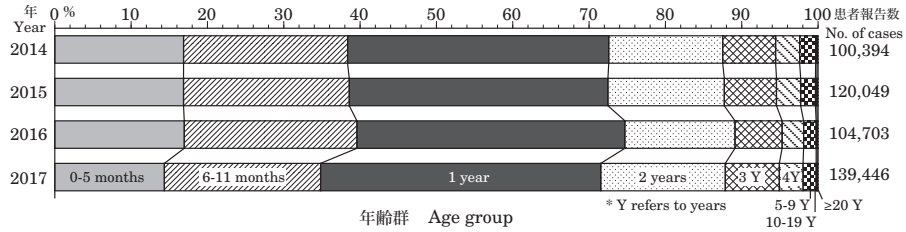

表1. RSウイルスが原因と届出された急性脳炎, 2014年1月～2018年9月

Table 1. Number of acute encepalitis/encephalopathy cases reported with RSV as the cause, January 2014-September 2018, Japan

診断年 Year of diagnosis	診断月 Month of diagnosis	診断時の年齢(歳) Age at diagnosis year	診断時の月齢(月) Age at diagnosis month	性別 Sex	診断年 Year of diagnosis	診断月 Month of diagnosis	診断時の年齢(歳) Age at diagnosis year	診断時の月齢(月) Age at diagnosis month	性別 Sex	診断年 Year of diagnosis	診断月 Month of diagnosis	診断時の年齢(歳) Age at diagnosis year	診断時の月齢(月) Age at diagnosis month	性別 Sex
2014	07	1		M	2015	12	1	3	F	2017	06	1	4	F
2014	10	2	11	F	2015	12	1		M	2017	06	3	8	M
2014	10	5	7	F	2016	02	2	10	M	2017	07	1		F
2014	10	5		F	2016	03	6	6	F	2017	07	1		F
2014	11	2		F	2016	07	3		M	2017	09	4		F
2014	12	1		M	2016	09	1		M	2017	10	2	2	M
2015	01	2		M	2016	09	3		F	2017	10	2	6	M
2015	03	1	1	F	2016	10	1		M	2018	01	1	10	M
2015	03	1		M	2016	10	2	10	M	2018	01	1		M
2015	07	1	7	F	2016	10	2		F	2018	05	1		F
2015	09	1	8	F	2016	11	1	6	M	2018	05	1		M
2015	10	5		F	2016	11	1		F	2018	06	2		M
2015	11	2	7	F	2016	12	2	2	M	2018	07	1	6	F
2015	12	1	3	M	2017	04	1	7	M					

M: 男, F: 女

(感染症発生動向調査 : 2018年10月31日現在)

(National Epidemiological Surveillance of Infectious Diseases: as of 31 October 2018)

図4. 検体採取月別呼吸器系ウイルス (RSウイルス, インフルエンザウイルス, ヒトメタニューモウイルス) 検出状況, 2013/14～2017/18シーズン (病原微生物検出情報 : 2018年11月5日現在報告数)

Figure 4. Number of respiratory viruses detected from clinical specimens, by month of sample collection, 2013/14-2017/18 seasons, Japan (sampling season from September through August in the following year)

[Infectious Agents Surveillance System: as of 5 November 2018 from prefectural and municipal public health institutes (PHIs)]

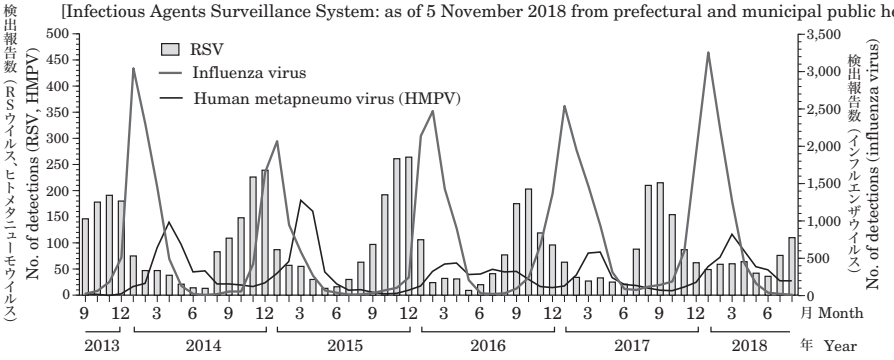

表2. 検体採取シーズン別呼吸器系ウイルス検出状況, 2013/14～2017/18シーズン

Table 2. Reported number of isolations/detections of respiratory viruses during the 2013/14-2017/18 seasons, Japan

検出ウイルス Virus	検体採取シーズン Sampling season* 2013/14	2014/15	2015/16	2016/17	2017/18	Total
Respiratory syncytial virus	1,033	1,073	1,154	1,094	1,014	5,368
Rhinovirus	1,737	1,783	1,830	1,741	1,717	8,808
Parainfluenza virus	734	695	581	591	590	3,191
Parainfluenza virus not typed	4	1	-	2	-	7
Parainfluenza virus 1	164	157	161	120	184	786
Parainfluenza virus 2	161	101	28	99	76	465
Parainfluenza virus 3	375	370	332	329	303	1,709
Parainfluenza virus 4	30	66	60	41	27	224
Human metapneumovirus	491	621	385	418	551	2,466
Human bocavirus	167	166	116	128	120	697
Human coronavirus	166	219	140	184	178	887
Influenza virus A not subtyped	4	12	7	27	15	65
Influenza virus A H1pdm09	3,496	64	3,659	382	2,321	9,922
Influenza virus A H3	1,739	5,232	636	7,648	3,270	18,525
Influenza virus B	2,969	873	3,314	1,810	4,606	13,572
Influenza virus C	30	3	65	1	57	156
Total	12,566	10,741	11,887	14,024	14,439	63,657

*インフルエンザシーズンによる (各年9月～翌年8月)　(病原微生物検出情報 : 2018年11月5日現在報告数)

*Sampling season from September through August in the following year

[Infectious Agents Surveillance System: as of 5 November 2018 from prefectural and municipal public health institutes (PHIs)]