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<THE TOPIC OF THIS MONTH>

Respiratory syncytial virus infection, as of May 2014

Respiratory syncytial virus (RSV) is an RNA virus belonging to *Pneumovirus* in *Paramyxoviridae* family (see p. 148 of this issue). It is propagated as droplet or contact infections. Estimatedly, more than 50% of infants acquire primary infection during the first year of life and nearly 100% before their second birthday. No first infection confers lifelong immunity (see p. 141 of this issue).

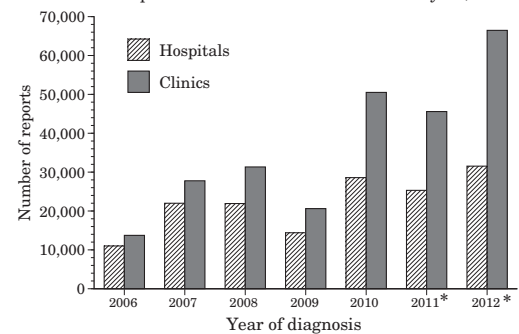
RSV infection occupies 50% of pneumonia and 50-90% of bronchiolitis among infants (see p. 139 & 142 of this issue). The clinical manifestation is indistinguishable from other respiratory virus infections. Therefore, laboratory diagnosis is indispensable for differential diagnosis. Clinical treatment of the patients is basically supportive.

Newborn, infant and immunocompromised cases tend to become serious (see pp. 139 & 150 of this issue) with development of apnea, syndrome of inappropriate antidiuretic hormone (SIADH), acute encephalopathy and other complications. Adult cases are generally mild (with flu-like symptoms) though they may transmit RSV to others. Aged cases may develop pneumonia as severe as that associated with influenza, and their case fatality rate is high (see p. 147 of this issue). Preventive measures against nosocomial RSV infection including early diagnosis should be implemented in facilities for elderlies or persons with disabilities, as RSV outbreaks have been reported from such facilities (see pp. 145 & 146 of this issue).

Currently, no preventive vaccines against RSV infection are available, though a humanized monoclonal antibody to RSV F glycoprotein, palivizumab, (developed in the USA and commercially available in Japan since 2002) is administered to high risk groups, such as, premature babies, patients with chronic pulmonary or congenital heart disease(s) for preventing RSV infection.

RSV infection is a category V infectious disease under the Infectious Diseases Control Law since its amendment in 2003. In compliance with the Law and under the framework of the National Epidemiological Surveillance of Infectious Diseases (NESID), pediatric sentinels report the notified RSV cases every week to the local public health centers. Notification requires laboratory diagnosis in-

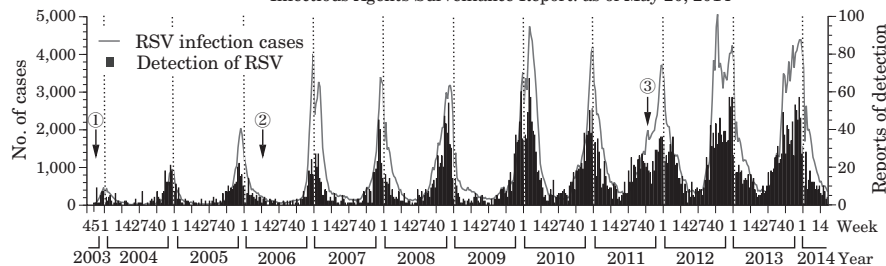
Figure 1. Number of reports of RSV infection cases by hospitals or by clinics, 2006-2012
(National Epidemiological Surveillance of Infectious Diseases: Number of reports at the end of each surveillance year)



| Year | 2006 | 2007 | 2008 | 2009 | 2010 | 2011* | 2012* |
|-----------|-------|-------|-------|-------|-------|-------|-------|
| Hospitals | 469 | 536 | 551 | 509 | 568 | 593 | 628 |
| Clinics | 790 | 1,009 | 1,102 | 1,046 | 1,400 | 1,635 | 1,864 |
| Total | 1,259 | 1,545 | 1,653 | 1,555 | 1,968 | 2,228 | 2,492 |

*118 cases in 2011 and one case in 2012 whose classification unknown are excluded.

Figure 2. Weekly number of RSV infection cases* and RSV detections**, week 45 of 2003- week 19 of 2014 * National Epidemiological Surveillance of Infectious Diseases: as of May 14, 2014 ** Infectious Agents Surveillance Report: as of May 20, 2014



※ Patients whose RSV antigen tests are covered by the medical insurance

① Hospitalized patients less than 3 years of age: since 2003

② All the hospitalized patients: since April 2006

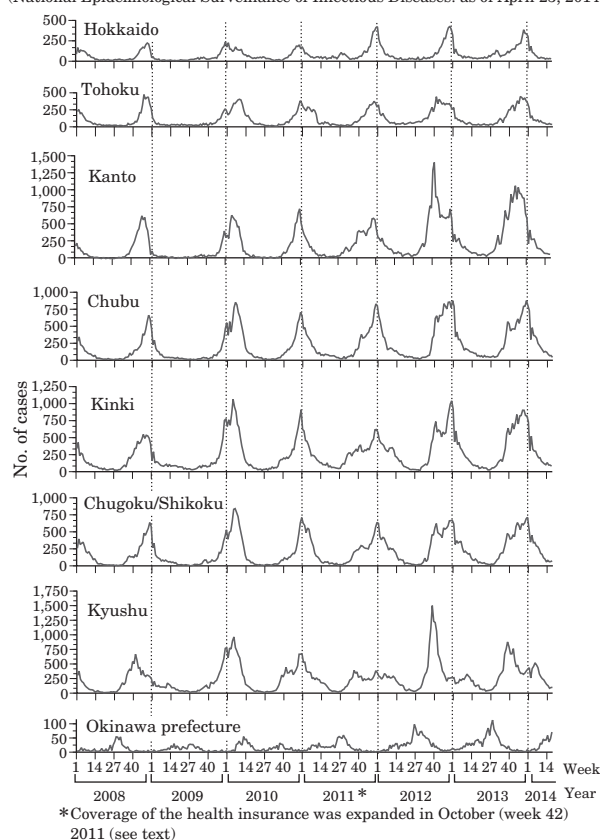
③ All the hospitalized patients and the outpatients who are infants and/or patients to whom palivizumab is indicated: since 17 October 2011

(Continued on page 138')

(THE TOPIC OF THIS MONTH-Continued)

Figure 3. Weekly cases of RSV infection by region, week 1 of 2008-week 16 of 2014, Japan

(National Epidemiological Surveillance of Infectious Diseases: as of April 23, 2014)



clinics doubled from 2008 to 2012 (Fig. 1).

RSV infections under NESID: During 2012-2013, the RSV infection epidemic started in July; the patients increased rapidly in September; the epidemic reached the peak towards the end of the year; and it continued till spring (Fig. 2). Osaka Prefecture continuously reported the highest number of patients (IASR 29: 271-273, 2008), followed by Hokkaido, Tokyo, Aichi and Fukuoka prefectures; they are all prefectures with high annual number of births. The epidemic season started earlier in Kyushu region. Okinawa Prefecture, differently from other regions, had the epidemic peak in summer (Fig. 3). From 2012 to 2013, there were 105,174 male patients (54%) and 89,370 female patients (46%). Infants under 2 years of age occupied 90% of the patients; the frequency proportion among <2 year patients was in the order of 0 year, 1 year and 2 years (Fig. 4 in p. 139 of this issue).

Since 2008, 22 RSV-related acute encephalopathy cases including 2 fatal cases (10 males, 12 females; 17 patients less than 2 years of age) have been reported. The patients' age ranged from 5 months to 13 years (median 2 years), which corresponds to the age groups whose RSV infection tends to be serious (Table 1).

Detection of RSV and other respiratory infectious viruses: Prefectural and municipal public health institutes (PHIs) isolate/detect virus from specimens sent from pathogen sentinels [corresponding about 10% of influenza sentinels (3,000 pediatric and 2,000 internal medicine clinics) and 500 sentinel hospitals]. Until 2009/10 influenza season, RSV was the second highest in detection frequencies following influenza, but since 2010/11 season, rhinovirus detections exceeded RSV detections (Table 2 in p. 139 of this issue). RSV was isolated/detected from autumn to winter; influenza in winter; and rhinovirus throughout the year (Fig. 5 in p. 139 of this issue). Human metapneumovirus and parainfluenza viruses (see p. 157 of this issue), though small in number, were isolated/detected most frequently from spring to summer.

In 2008/09-2013/14 season, 57 PHIs in 44 prefectures isolated/detected RSV from 5,441 cases (as of 20 May 2014). The most frequent RSV-positive specimens were throat swab (5,358 specimens, 98%) and the most frequent detection method applied was PCR (4,959 cases, 91%) followed by cell culture isolation (932 cases, 17%), and antigen detection (49 cases, 1%) (detection by more than one method included). The most frequent respiratory disease-related diagnosis of the cases from which the specimens were collected was lower respiratory tract inflammation (2,371 cases, 44%) followed by RSV infection (1,746 cases, 32%) and upper respiratory tract inflammation (495 cases, 9%).

Challenges in future: RSV infection is associated with high incidence of pneumonia among aged groups and serious complications among infants. To reduce the disease burden, the RSV surveillance system should be strengthened to make evidence based intervention possible.

Table 1. Acute encephalopathy cases due to respiratory syncytial virus, Japan, 2008-2013

| Year | Month of diagnosis | Age (years) | Gender | Remarks |
|------|--------------------|-------------|--------|---------|
| 2008 | December | 2 | Female | |
| | March | 2 | Male | Dead |
| 2009 | December | 2 | Male | |
| | December | 2 | Male | |
| | January | 1 | Male | |
| 2010 | February | 2 | Male | |
| | February | 1 | Male | |
| | September | 1 | Female | |
| | September | 13 | Female | |
| 2011 | February | 5 | Male | |
| | April | 3 | Female | |
| | June | 1 | Female | |
| | July | 11 | Female | |
| 2012 | December | 2 | Female | |
| | January | 2 | Male | |
| | April | 0 (8 mo.) | Female | Dead |
| | July | 0 (5 mo.) | Female | |
| 2013 | November | 2 | Male | |
| | September | 0 (11 mo.) | Female | |
| | November | 6 | Male | |
| | December | 1 | Female | |
| 2013 | December | 0 (10 mo.) | Female | |

(National Epidemiological Surveillance of Infectious Diseases: as of April 24 2014)

cluding RSV antigen detection (notification criteria in <http://www.niid.go.jp/niid/images/iasr/35/412/de4121.pdf>). Though it had been limited to hospitalized patients before 17 October 2011, the medical insurance now covers RSV antigen detection testing of infants and other outpatients, to whom palivizumab is indicated (see p. 143 of this issue). Among approximately 3,000 pediatric sentinels (hospitals and clinics), now about 80% of them report RSV infection. In particular, clinics without beds increasingly report RSV infection cases in recent years, and the number of RSV infection reporting from such

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 Law Concerning the Prevention of Infectious Diseases and Medical Care for Patients of Infections, and 2) other data covering various aspects of infectious diseases. The prefectural and municipal health centers and public health institutes (PHIs), the Department of 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)

図4. RSウイルス感染症患者の年齢分布, 2008~2013年 (感染症発生動向調査: 2014年4月25日現在報告数)

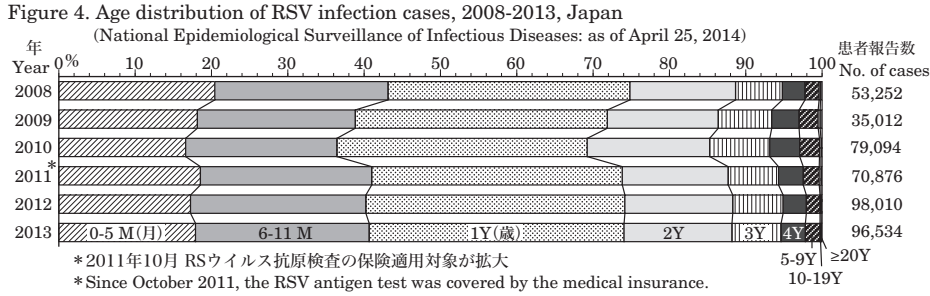


表2. 検体採取シーズン別呼吸器系ウイルス検出状況, 2007/08~2013/14シーズン

Table 2. Respiratory viruses during 2007/08-2013/14 seasons

| 検出ウイルス Virus | 検体採取シーズン* Sampling season* | | | | | | | 合計 Total |
|-------------------------------|----------------------------|---------|---------|---------|---------|---------|---------|----------|
| | 2007/08 | 2008/09 | 2009/10 | 2010/11 | 2011/12 | 2012/13 | 2013/14 | |
| Respiratory syncytial virus | 412 | 535 | 974 | 939 | 975 | 1,164 | 854 | 5,853 |
| Rhinovirus | 226 | 238 | 645 | 1,282 | 1,670 | 1,581 | 991 | 6,633 |
| Parainfluenza virus | 204 | 338 | 521 | 580 | 729 | 764 | 278 | 3,414 |
| Parainfluenza virus not typed | 2 | 13 | 4 | 1 | 36 | 8 | 1 | 65 |
| Parainfluenza virus 1 | 43 | 62 | 129 | 121 | 230 | 222 | 113 | 920 |
| Parainfluenza virus 2 | 17 | 55 | 102 | 62 | 69 | 100 | 100 | 505 |
| Parainfluenza virus 3 | 141 | 207 | 276 | 381 | 318 | 397 | 39 | 1,759 |
| Parainfluenza virus 4 | 1 | 1 | 10 | 15 | 76 | 37 | 25 | 165 |
| Human metapneumovirus | 266 | 244 | 467 | 547 | 545 | 547 | 215 | 2,831 |
| Human bocavirus | 35 | 40 | 68 | 206 | 233 | 162 | 61 | 805 |
| Coronavirus | 1 | - | 16 | 96 | 61 | 118 | 127 | 419 |
| Influenza virus A H unknown | - | 8 | 12 | 2 | 14 | 15 | 4 | 55 |
| Influenza virus A H1pdm09 | n/a | 9,866 | 22,130 | 6,257 | 15 | 163 | 3,305 | 41,736 |
| Influenza virus A H1 | 3,819 | 3,607 | - | - | - | - | - | 7,426 |
| Influenza virus A H3 | 544 | 2,663 | 157 | 3,862 | 5,143 | 5,046 | 1,620 | 19,035 |
| Influenza virus B | 330 | 2,039 | 194 | 1,848 | 2,043 | 1,465 | 2,592 | 10,511 |
| Influenza virus C | 24 | 9 | 52 | 12 | 61 | 2 | 9 | 169 |
| 合計 Total | 5,861 | 19,587 | 25,236 | 15,631 | 11,489 | 11,027 | 10,056 | 98,887 |

*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: 2014年5月20日現在報告数)
* Sampling season is adjusted to that of influenza virus, which is from September to August of the next year.
n/a: not applicable 該当なし

(Infectious Agents Surveillance Report: as of May 20, 2014)

図5. 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, ライノウイルス) 検出状況, 2008/09~2013/14シーズン (病原微生物検出情報: 2014年5月1日現在報告数)

Figure 5. Monthly number of respiratory viruses (RSV, influenza virus and rhinovirus) detections from clinical specimens, 2008/09-2013/14 seasons (Infectious Agents Surveillance Report: as of May 1, 2014)

