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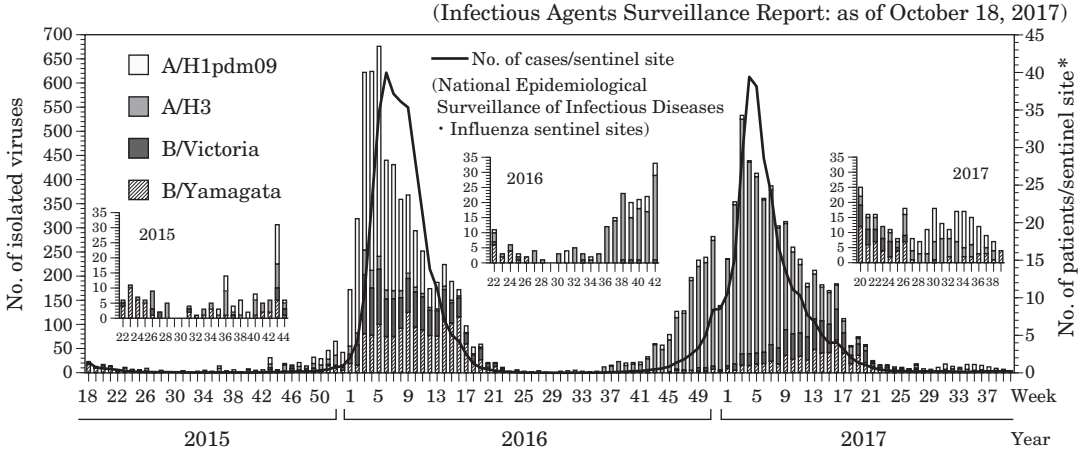
National Institute of Infectious Diseases and Tuberculosis and Infectious Diseases Control Division, Ministry of Health, Labour and Welfare



## <THE TOPIC OF THIS MONTH>
## Influenza 2016/17 season, Japan

Figure 1. Weekly number of isolated influenza viruses and reported influenza patients/sentinel site from week 18, 2015 to week 40, 2017, Japan
(Infectious Agents Surveillance Report: as of October 18, 2017)




*Indicator of the nationwide start of influenza season: 1.0

The 2016/17 influenza season (from week 36 in September 2016 to week 35 in August 2017) was characterized by the predominance of the A/H3 subtype, with a smaller contribution by both the Yamagata and Victoria lineages of influenza type B.

**Epidemiology of the 2016/17 influenza season**: Under the National Epidemiological Surveillance of Infectious Diseases (NESID) system, approximately 5,000 influenza sentinel sites (approximately 3,000 pediatric and 2,000 internal medicine health facilities) report patients diagnosed as influenza on a weekly basis. The number of patients reported per sentinel exceeded 1.0 (indicator of the nationwide start of influenza season) in week 46 of 2016 (Fig. 1) (http://www.niid.go.jp/niid/en/10/2096-weeklygraph/2572-trend-week-e.html) and exceeded 10.0 (indicator for the alert level, used at the prefectural level) in all 47 prefectures by week 3 of 2017. The peak was in week 4 of 2017 with 39.4 patients/sentinel. In Okinawa Prefecture, for the first time in the past five influenza seasons, there was a week in July when influenza reports exceeded 10.0 patients/sentinel (see p. 226 of this issue).

Based on the reported sentinel surveillance data, the estimated number of influenza patients who attended medical facilities from week 36 of 2016 to week 20 of 2017 (from September 5, 2016 to May 21, 2017) was 16,960,000. According to hospitalized influenza patient surveillance (data from approximately 500 designated sentinel hospitals with ≥300 beds), the number of hospitalized influenza patients during the same period was 15,405, which was 1.25-fold greater than that in the 2015/16 season (12,275 patients). Among patients diagnosed as "acute encephalitis" (a category V notifiable infectious disease), 117 were reported as cases whose causative pathogen was influenza virus (as of May 15, 2017), which was about half of that reported in the previous season (224 in the 2015/16 season). Other information, such as excess mortality data, are reported in the 2016/17 annual influenza season report (https://www.niid.go.jp/niid/images/idsc/disease/influ/fludoco1617.pdf, in Japanese).

**Isolation/detection of influenza virus**: In the 2016/17 season, prefectural and municipal public health institutes (PHIs) reported a total of 9,578 isolations/detections of influenza viruses (6,804 isolations and 2,774 detections without isolation) (Table 1 in p. 211 of this issue). Among them, 8,514 were reported from the influenza sentinel sites and 1,064 from non-sentinel sites (Table 2 in p. 211). A/H3 made up 78%, influenza type B 18% (Yamagata lineage 44%, Victoria lineage 56%) and A/H1pdm09 4% (Table 2). The number of A/H3 isolations began increasing from week 42 of 2016 and peaked in week 3 of 2017. Influenza type B isolations increased from week 3 of 2017 and surpassed that of influenza type A after week 14 of 2017 (Fig. 1 and Fig. 2 in p. 211). In all the age groups, A/H3 was found more frequently than A/H1pdm09 or type B (https://www.niid.go.jp/niid/ja/flu-m/1974-idsc/iasr-flu/7646-influ201617.html).

**Genetic and antigenic characteristics of 2016/17 isolates**: The National Institute of Infectious Diseases (NIID) conducts

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genetic and antigenic analysis of isolates from Japan and other Asian countries. For the antigenic analysis, the sera obtained from infected ferrets were used (see p. 212 of this issue).

Almost all the A/H1pdm09 isolates analyzed belonged to genetic clade 6B.1. While isolates tested antigenically resembled A/California/7/2009 (2016/17 season vaccine strain), when human post-vaccination sera were used, recent A/H1pdm09 isolates more closely resembled A/Michigan/45/2015 (the representative strain for clade 6B.1), suggesting antigenic difference between the circulating viruses and the vaccine strain.

All A/H3 isolates analyzed belonged to genetic clade 3C.2a, and 60% of them to subclade 3C.2a1. Antigenically, 50-60% of isolates tested resembled A/Hong Kong/4801/2014 (the vaccine strain for the 2016/17 season).

All B/Yamagata lineage isolates analyzed belonged to genetic clade 3, and most of isolates tested antigenically resembled B/Phuket/3073/2013 (the vaccine strain for the 2016/17 season). All B/Victoria lineage strains belonged to genetic clade 1A and most of them tested antigenically resembled B/Texas/2/2013 (the vaccine strain for the 2016/17 season). In the 2016/17 season, antigenic variants possessing amino acid deletions in hemagglutinin (HA) protein were detected among B/Victoria lineage isolates from the US and other countries; it will thus be important to maintain vigilance also in Japan (p. 212 of this issue).

**Resistance to antivirals among 2016/17 isolates**: Among 238 A/H1pdm09 isolates from Japan, resistance to both oseltamivir and peramivir was found in 3 isolates. All A/H3 isolates, from Japan (478 isolates), were sensitive to oseltamivir, peramivir, zanamivir and laninamivir. All the 360 influenza type B isolates from Japan were sensitive to these antivirals (see p. 212 of this issue).

**Seroprevalence among the Japanese population**: Under the Preventive Vaccination Law, since April 1, 2013, seroprevalence surveys have been conducted to monitor immunity levels (see p. 221 of this issue). The data were obtained from 5,883 serum samples collected ahead of the 2016/17 season (i.e. from July to September 2016). The age groups with the highest seroprevalence (measured as HI antibody positive, titer ≥1:40) were 5-29 year olds (78-90%) for A/California/7/2009 [A(H1N1)pdm09], 5-19 year olds (65-73%) for A/Hong Kong/4801/2014 [A(H3N2)], and 20-29 year olds (63-64%) for B/Phuket/3073/2013 (B/Yamagata lineage). The sero-positivity to B/Texas/2/2013 (B/Victoria lineage) was less than 40% for all age groups.

**Influenza vaccine**: The tetravalent vaccine for the 2016/17 season contained antigens of two type A and two type B strains. Approximately 27,840,000 vial-equivalent doses (estimated on the assumption that 1 vial contained 1 mL) were produced in the 2016/17 season, of which an estimated 26,420,000 vials were used.

For the 2017/18 season, the A/H1 strain selected was A/Michigan/45/2015-like A/Singapore/GP1908/2015(IVR-189), which had high production efficiency; the A/H3 strain selected was A/Hong Kong/4801/2014 (X-263) as in the 2016/17 season; and the B/Yamagata and B/Victoria strains selected were B/Phuket/3073/2013 and B/Texas/2/2013, respectively, as in the previous season (see p. 225 of this issue).

The multicenter test-negative design case-control studies conducted in the 2013/14 to 2015/16 seasons demonstrated that, for each respective season, two vaccine shots to children under 6 years of age was significantly associated with reduced occurrence of symptomatic influenza infection (see p. 223 of this issue).

**Human infection with avian or swine influenza virus**: As of 27 September 2017, 860 confirmed human cases (455 fatal cases) of highly pathogenic avian influenza A(H5N1) virus infections have been reported from 16 countries since 2003. And, since 2014, China has reported 14 human cases of A(H5N6) virus infections. In addition, since 2013, China has reported many human cases of low pathogenic avian influenza A(H7N9) virus infections, with a total of 1,562 human cases (608 fatal cases) as of 13 September 2017. During the fifth epidemic wave (October 2016 to September 2017) of this virus, 764 human cases (288 fatal cases) were reported; in addition, highly pathogenic A(H7N9) viruses recently emerged and were also detected for the first time from human cases. Cases of human infections with avian influenza A(H9N2) virus have been sporadically reported from China and Egypt.

As for swine influenza viruses, sporadic transmissions of the virus from pigs to humans have been reported from agricultural fairs in the United States [e.g. A(H3N2) variant (v), A(H1N1)v, and A(H1N2)v viruses] (see p. 218 of this issue).

**Conclusion**: Response to influenza will require sustained, comprehensive monitoring. Important activities include monitoring of trends in the occurrence of influenza patients, isolation of influenza viruses, analysis of the antigenic and genetic properties of circulating strains, vigilance against emergence of drug-resistant strains, and monitoring of seroprevalence levels. Preliminary data on the isolation and detection of influenza viruses in the 2017/18 influenza season are available in p. 227 of this issue and at http://www.niid.go.jp/niid/en/iasr-inf-e.html.

**Note:** For IASR reporting, influenza nomenclature is based on the virus information available. Influenza viruses are classified by type, subtype and strains, based on the hemagglutination (HA), neuraminidase (NA) and other information:

- When both HA and NA typing have been performed, names are listed fully [e.g. A(H1N1)pdm09, A(H3N2), A(H5N1)].
- When NA typing has not been performed, only HA information is listed (e.g. A/H1pdm09, A/H3).
- Strain name is represented by location of isolation; in case of isolation in Japan, the location is written in Japanese kanji, and in case of isolation in foreign countries, in English.
- To distinguish swine influenza viruses recovered from humans from seasonal influenza viruses, the term“variant virus” is used with a letter “v” added after the subtype name [e.g. A(H3N2)v].

*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 Environmental Health and Food Safety, the Ministry of Health, Labour and Welfare, and quarantine stations, have provided the above data.*

**Infectious Disease Surveillance Center, National Institute of Infectious Diseases**
Toyama 1-23-1, Shinjuku-ku, Tokyo 162-8640, JAPAN Tel (+81-3)5285-1111

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

表1．インフルエンザウイルス分離・検出報告数，2013/14〜2016/17シーズン
Table 1. Isolation/detection of influenza viruses during the 2013/14-2016/17 influenza seasons

| 型 Type | シーズン* Season* 2013/14 | 2014/15 | 2015/16 | 2016/17 |
|---|---|---|---|---|
| A/H1pdm09 | 2,847 （ 649） | 41 （ 22） | 3,032 （ 608） | 261 （ 100） |
| A/H3 | 1,204 （ 535） | 3,701 （ 1,530） | 415 （ 217） | 5,154 （ 2,321） |
| A NT | − （ 4） | − （ 12） | 1 （ 6） | 1 （ 26） |
| B/Victoria | 627 （ 116） | 57 （ 8） | 1,174 （ 198） | 780 （ 115） |
| B/Yamagata | 1,656 （ 278） | 653 （ 104） | 1,526 （ 234） | 606 （ 102） |
| B NT | 20 （ 272） | 11 （ 39） | 2 （ 146） | 2 （ 109） |
| C | 21 （ 9） | 2 （ 1） | 22 （ 43） | − （ 1） |
| 合計 Total | 6,375 （ 1,863） | 4,465 （ 1,716） | 6,172 （ 1,452） | 6,804 （ 2,774） |

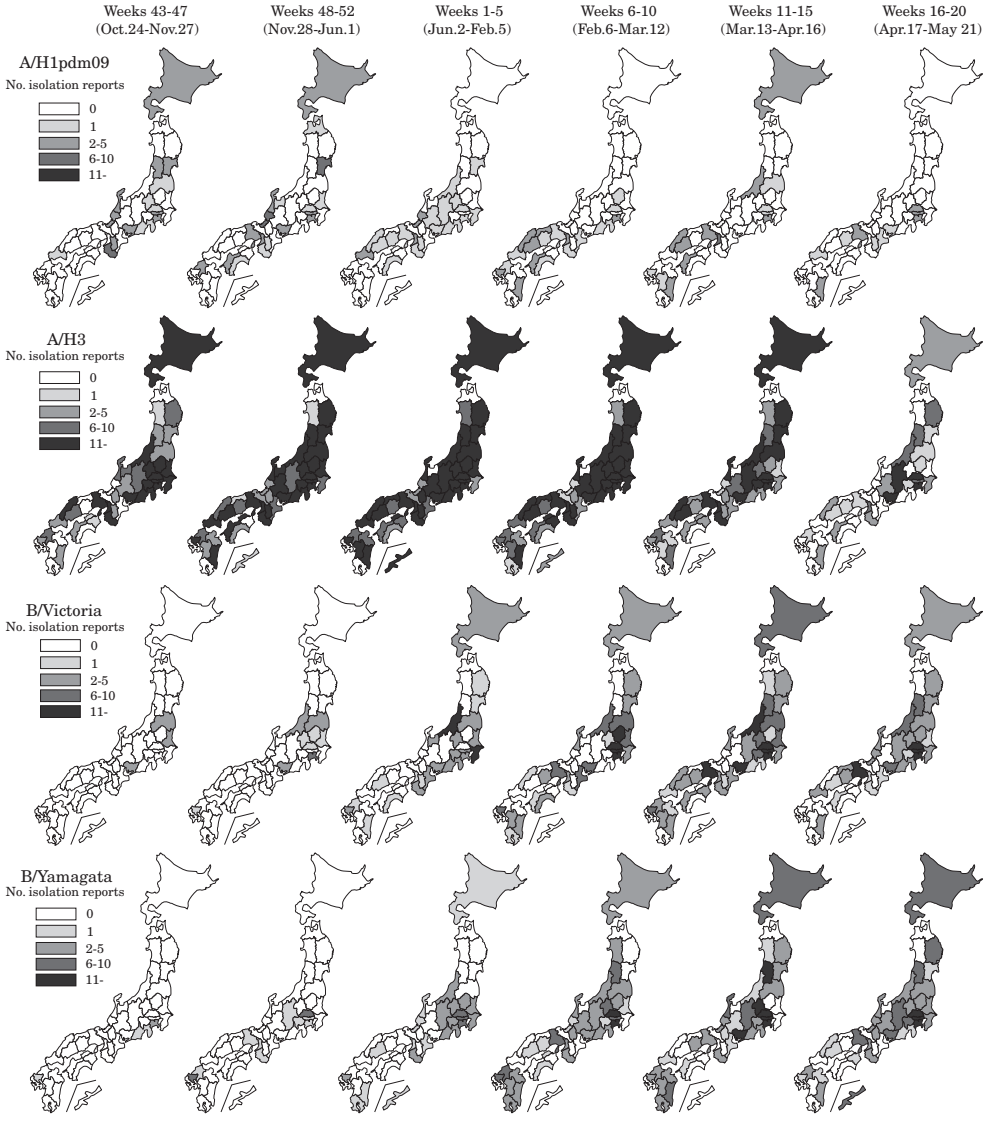
A NT: A亜型未同定, B NT: B系統未同定
A NT: A not subtyped, B NT: B lineage not determined
*各シーズン(当年9月〜翌年8月)に採取された検体から各地方衛生研究所で分離されたウイルス報告数, −報告なし, （ ）内はウイルスは分離されていないが, 遺伝子検出または抗原検出による報告数を別掲
（病原微生物検出情報：2017年10月15日現在報告数）
*Sampling season from September through August in the following year.
( ): Nos. in parentheses denote gene or antigen detection without isolation, not included in the total.
[Infectious Agents Surveillance Report: as of October 15, 2017 from prefectural and municipal public health institutes (PHIs)]

表2．インフルエンザウイルス分離・検出報告数，2016/17シーズン
Table 2. Isolation/detection of influenza viruses during the 2016/17 influenza season

| 型 Type | Total (a+b) | (a) | (b) |
|---|---|---|---|
| A/H1pdm09 | 361 | 298 | 63 |
| A/H3 | 7,475 | 6,563 | 912 |
| A NT | 27 | 21 | 6 |
| B/Victoria | 895 | 856 | 39 |
| B/Yamagata | 708 | 667 | 41 |
| B NT | 111 | 109 | 2 |
| C | 1 | − | 1 |
| 合計 Total | 9,578 | 8,514 | 1,064 |

(a) インフルエンザ定点（小児科+内科）
Reports from influenza sentinels (pediatric & internal medicine sites)
(b) インフルエンザ定点以外（基幹定点+その他）
Reports from sites other than influenza sentinels
A NT: A亜型未同定, B NT: B系統未同定
A NT: A not subtyped, B NT: B lineage not determined
2016年9月〜2017年8月に採取された検体から各地方衛生研究所で分離・検出されたウイルス報告数, −報告なし
（病原微生物検出情報：2017年10月15日現在報告数）
Based on samples collected from September 2016-August 2017.
(Infectious Agents Surveillance Report: as of October 15, 2017 from PHIs)

図2．都道府県別インフルエンザウイルス分離報告状況，2016/17シーズン
Figure 2. Isolation of influenza viruses by prefecture during the 2016/17 influenza season




（病原微生物検出情報：2017年10月18日現在報告数）(Infectious Agents Surveillance Report: As of October 18, 2017 from PHIs)