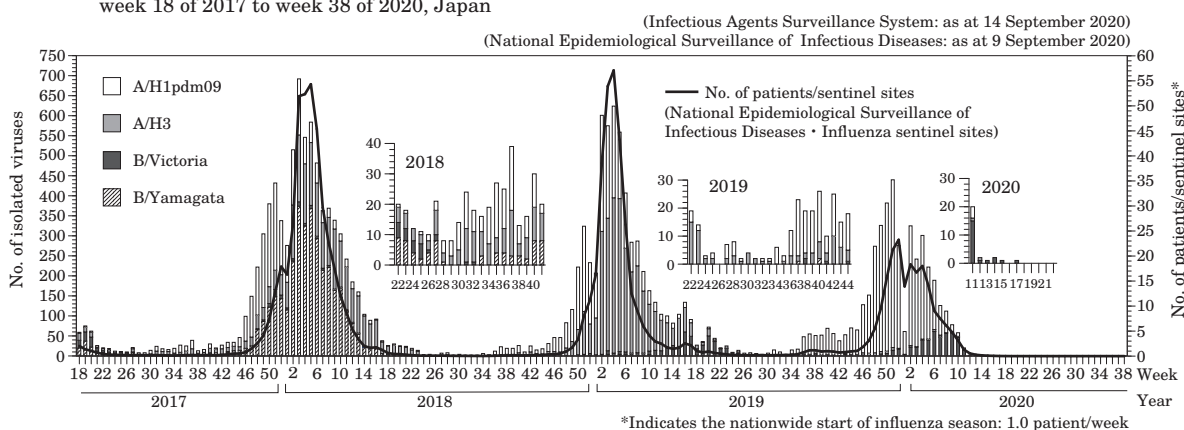


Trend in occurrence of influenza in the 2019/20 season in Okinawa Prefecture.....	194	Effectiveness of influenza vaccine among children younger than 3 years: summary from the 2018/19 influenza season (report from the MHLW-funded study group)	204
Analysis of influenza viruses isolated in the 2019/20 influenza season, Japan.....	195	Update on avian and swine influenza virus infections among humans....	206
The detection and characteristics of antiviral drug-resistant influenza viruses, Japan.....	200	Estimates of Excess deaths during the COVID-19 pandemic: notes on interpretation and future directions	207
Influenza vaccination coverage and seroprevalence of influenza, Japan-FY 2019, National Epidemiological Surveillance of Vaccine-Preventable Diseases.....	201	Influenza in the southern hemisphere temperate regions in the 2020 winter season	208
		<i>Legionella</i> spp. detected in mud from the typhoon Hagibis stricken area in 2019	210

<THE TOPIC OF THIS MONTH> Influenza 2019/20 season, Japan

Figure 1. Weekly number of isolated influenza viruses and reported influenza patients/sentinel site, week 18 of 2017 to week 38 of 2020, Japan



The 2019/20 influenza season (from week 36 in September 2019 to week 35 in August 2020) was characterized by the predominance of the influenza A/H1pdm09 subtype, and influenza B, mainly Victoria lineage, also increased from week 51 in 2019.

Epidemiology of the 2019/20 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 facilities) report patients diagnosed as influenza on a weekly basis. The number of patients reported per sentinel exceeded 1.0 (the usual indicator of the nationwide start of influenza season) in week 37 (September 9-15) of 2019 due to a local epidemic of mainly influenza A in Okinawa Prefecture (see p.194 of this issue), but the nationwide influenza season was considered to have started in week 45 (November 4-10) of 2019 (Fig. 1 & <https://www.niid.go.jp/niid/ja/10/weeklygraph.html>).

In week 52 (December 23-29), the number exceeded the alert level of 10.0 in all 47 prefectures and the peak was also in the same week (23.24 patients/sentinel, which was approximately half the value of the average year's peak).

Based on the reported sentinel surveillance data, the estimated number of influenza patients who visited medical facilities (between week 36 of 2019 and week 17 of 2020) was approximately 7,289,000, approximately 61% of that during the same period in the previous season (12,005,000). According to hospitalized influenza patient surveillance (data from approximately 500 designated sentinel hospitals with ≥ 300 beds), the number of hospitalized influenza patients was 12,982, approximately 64% of that during the same period in the previous season. Among patients diagnosed with acute encephalitis (including encephalopathy), a category V notifiable infectious disease, 254 were diagnosed with influenza encephalitis, the largest number in the past three seasons (<https://www.niid.go.jp/niid/images/idsc/disease/influ/fludoco1920.pdf>).

Nationwide excess deaths in the 2019/2020 season and January-June 2020 when the COVID-19 pandemic started were analyzed by two algorithms used in the US and Europe, estimating 191-4,577 and 319-7,467, respectively (see p.207 of this issue).

Isolation/detection of influenza virus in the 2019/20 season: Prefectural and municipal public health institutes (PHIs) reported the isolation/detection of 5,929 influenza viruses (4,291 isolates and 1,638 detections without isolation) (Table 1). Among them, 5,478 were reported from influenza sentinel sites and 451 from non-sentinel sites (Table 2). Influenza type A/H1pdm09 comprised 85%, A/H3 comprised 2%, and type B comprised 12% (Victoria lineage 98.7%, Yamagata lineage 0.6%, and unknown lineage 0.7%) (Table 2). Although isolations of A/H1pdm09 increased from week 46 (November 11-17) of 2019, those of type B Victoria lineage started to increase from week 51 (December 16-22) of 2019, surpassing those of type A from week 9 (February 24-March 1) of 2020 (Fig. 1 & Fig. 2). As for the winter season in the temperate region of the southern hemisphere, no epidemic was observed even in May-August when the epidemic usually peaks (see p.208 of this issue).

Genetic and antigenic characteristics of 2019/20 isolates: The National Institute of Infectious Diseases (NIID) conducted genetic and antigenic analyses of isolates from Japan and other Asian countries; antigenic analyses were done using ferret antiserum

(Continued on page 192')

(THE TOPIC OF THIS MONTH-Continued)

(p.195 of this issue). The hemagglutinin (HA) genes of all A/H1pdm09 isolates analyzed belonged to genetic clade 6B.1A, and the majority of viruses possessed 183P substitution in HA.

Although A/H3 strains are largely divided into two groups, 3C.2a and 3C.3a, in the HA gene tree, the dominant strains analyzed in the 2019/20 season belonged to 3C.2a, as in the past five seasons. Within genetic clade 3C.2a, many subclades were formed, representing genetic diversification. Antigenic analysis revealed that almost all strains tested were antigenically different from cell culture-propagated A/Kansas/14/2017 (clade 3C.3a), the vaccine strain for the 2019/20 season (demonstrated 8-fold or greater reduction in virus neutralization (VN) titer than homologous VN titer of A/Kansas/14/2017 virus).

Only two domestic strains of B/Yamagata lineage were analyzed and they were antigenically similar to B/Phuket/3073/2013 virus (the vaccine strain for the 2019/20 season). Although all of the B/Victoria lineage strains belonged to genetic clade 1A of the HA gene tree, 99% of the domestic strains belonged to genetic clade 1A.3, which has three amino acid deletions in HA. The antigenic analysis also revealed that more than 90% of isolates in the 2019/20 season reacted well with ferret antiserum against B/Colorado/06/2017 virus (WHO recommended vaccine strain for the 2019/20 season), which has two amino acid deletions in HA.

Resistance to antivirals among 2019/20 isolates: Regarding neuraminidase inhibitors (oseltamivir, peramivir, zanamivir, and laninamivir), among the 2,489 domestic isolates of A/H1pdm09, 40 (1.6%) were resistant to oseltamivir/peramivir. Twenty-eight of these strains were isolated from patients who had not received these drugs. Regarding a cap-dependent endonuclease inhibitor (Baloxavir), among the 831 domestic isolates of A/H1pdm09, 1 (0.12%) Baloxavir-resistant mutant was detected from a patient who had not received the drug. As for A/H3 and B, all domestic isolates analyzed and isolates from 5 Asian countries were susceptible to NA inhibitors and Baloxavir (see p.200 of this issue).

Seroprevalence among the Japanese population prior to the 2019/20 season: Based on seroprevalence surveys conducted under the National Epidemiological Surveillance of Vaccine-Preventable Diseases program, the seroprevalence levels were measured from 5,446 serum samples collected between July and September 2019 (see p.201 of this issue). The age groups with the highest seroprevalence (measured as HI antibody-positive, titer $\geq 1:40$) were 5-24-year-olds (57-60%) for A/Brisbane/02/2018 [A(H1N1)pdm09], 5-19-year-olds (53%) for A/Kansas/14/2017 [A(H3N2)], and 15-39-year-olds (60-70%) for B/Phuket/3073/2013 (B/Yamagata lineage). Compared to other age groups, seroprevalence for B/Maryland/15/2016 (B/Victoria lineage) was highest in 40-49-year-olds (51-52%).

Influenza vaccine: The tetravalent vaccine for the 2019/20 season contained antigens of two type A and two type B strains. Approximately 29,640,000 vial-equivalent doses (estimated on the assumption that 1 vial contained 1 mL) were produced, of which an estimated 28,250,000 vials were used.

For the 2020/21 season, A/Guangdong-Maonan/SWL1536/2019 (CNIC-1909) was selected as the A/H1 strain and A/Hong Kong/2671/2019 (NIB-121) as the A/H3 strain. As for the B/Yamagata strain, B/Phuket/3073/2013 was selected as in the 2019/20 season and B/Victoria/705/2018 (BVR-11) was selected for the B/Victoria strain (https://www.mhlw.go.jp/stf/shingi2/0000203023_00005.html). Active vaccination continues to be recommended.

A multicenter case-control study was performed on the effectiveness of two doses of the influenza vaccine, and for the 2018/19 season among children under three years of age, although not statistically significant, effectiveness against symptomatic influenza was observed (see p.204 of this issue).

Human infection with avian and swine influenza virus: From 2003 through March 2019, 861 confirmed human cases (455 fatal cases) of highly pathogenic avian influenza A(H5N1) virus infection were reported from 17 countries. Since October 2019, five countries, including China, reported cases of A(H5N1), four countries reported cases of A(H5N6), and 14 countries, including Japan, reported cases of A(H5N8). Since 2013, numerous human infection cases of avian influenza A(H7N9) have been reported in China, with a total of 1,568 cases (including 616 deaths). During the fifth epidemic from October 2016 to September 2017, A(H7N9) viruses that were highly pathogenic to poultry also emerged and human infection cases were reported, but no human infection case has been reported since the last case in March 2019. Human cases of avian influenza A(H9N2) virus infection have been sporadically reported from China, Egypt, Bangladesh, India, Senegal, and Oman.

Swine may play the role of an intermediate "mixing vessel" host, generating reassortments of avian and mammalian influenza viruses. Human cases of A(H3N2) variant (v), A(H1N1)v, and A(H1N2)v virus infections associated with exposure at agricultural fairs in the US have been reported; other swine influenza cases from Germany, China, and Brazil have also been reported. Swine influenza has also been detected in Japan and caution is needed (see p.206 of this issue).

Conclusion: The 2019/20 season saw an unprecedented decline in the reported number of influenza cases since the beginning of 2020. Care in interpretation is required, as this decrease may have been not only due to changes in individual-level behavior change or public health response measures, but also due to such aspects as refraining from visiting medical facilities, potentially affecting influenza activity and its relevant indicators. For the 2020/21 season, with the COVID-19 epidemic expected to continue, the impact of COVID-19 on influenza occurrence or virus detection is unclear--public health measures, including influenza vaccines, are being urgently put in place. At the same time, comprehensive monitoring through routine activities--such as the isolation/detection of influenza viruses, analyses of the antigenic and genetic properties of circulating strains, vigilance against the emergence of drug-resistant strains, and monitoring of population seroprevalence levels--will be ever more important. Further considerations on specific approaches will be necessary.

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.

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, 2016/17~2019/20シーズン
Table 1. Isolation/detection of influenza viruses during the 2016/17-2019/20 influenza seasons

型 Type	シーズン* Season*			
	2016/17	2017/18	2018/19	2019/20
A/H1pdm09	280 (102)	1,885 (454)	2,442 (639)	3,703 (1,363)
A/H3	5,299 (2,358)	2,309 (1,012)	3,323 (1,412)	93 (38)
A NT	1 (26)	- (15)	4 (10)	2 (3)
B/Victoria	814 (118)	112 (32)	473 (132)	477 (224)
B/Yamagata	656 (114)	3,479 (945)	37 (9)	3 (1)
B NT	2 (109)	6 (52)	6 (6)	- (5)
C	- (1)	40 (17)	1 (2)	13 (4)
合計 Total	7,052 (2,828)	7,831 (2,527)	6,286 (2,210)	4,291 (1,638)

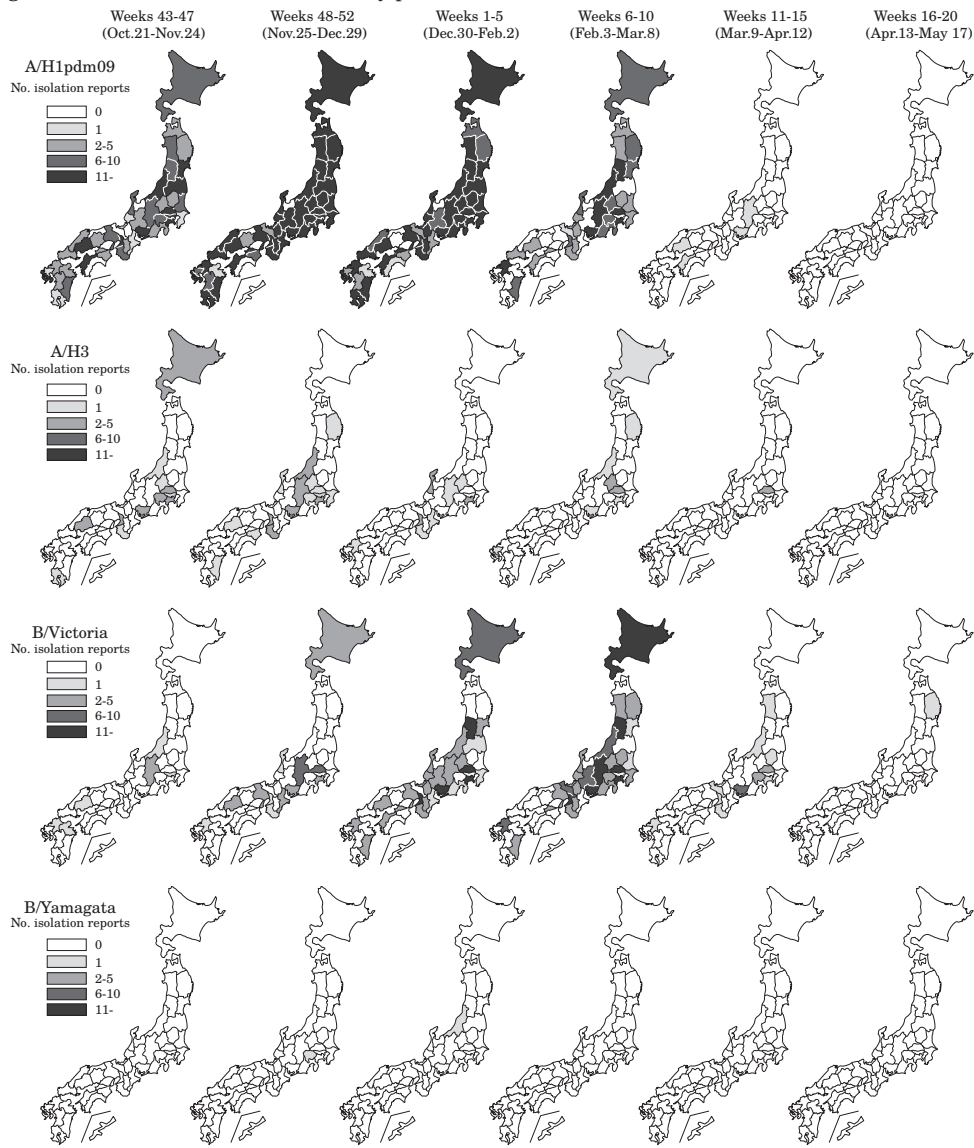
A NT: A亜型未同定, B NT: B系統未同定
A NT: A not subtyped, B NT: B lineage not determined
*各シーズン(当年9月~翌年8月)に採取された検体から各地方衛生研究所で分離されたウイルス報告数, -報告なし, ()内はウイルスは分離されていないが, 遺伝子検出または抗原検出による報告数を別掲 (病原微生物検出情報: 2020年9月14日現在報告数)
* Sampling season from September through August in the following year.
(): Nos. in parentheses denote gene or antigen detection without isolation, not included in the total.
[Infectious Agents Surveillance System: as at 14 September 2020 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, 2019/20シーズン
Table 2. Isolation/detection of influenza viruses during the 2019/20 influenza season

型 Type	Total (A+B)	(A)	(B)
A/H1pdm09	5,066	4,656	410
A/H3	131	107	24
A NT	5	5	-
B/Victoria	701	686	15
B/Yamagata	4	3	1
B NT	5	5	-
C	17	16	1
合計 Total	5,929	5,478	451

(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
2019年9月~2020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: 2020年9月14日現在報告数)
Based on samples collected from September 2019-August 2020.
(Infectious Agents Surveillance System: as at 14 September 2020 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, 2019/20シーズン
Figure 2. Isolation of influenza viruses by prefecture in the 2019/20 influenza season



(病原微生物検出情報: 2020年9月14日現在報告数)
(Infectious Agents Surveillance System: as at 14 September 2020 from PHIs)

注) IASRのインフルエンザウイルス型, 亜型, 株名の記載方法は, 赤血球凝集素 (HA) の分類を調べた情報を主とする場合と, さらにノイラミニダーゼ (NA) の型別まで実施された場合などの違いによるものである。
・N型別まで実施されている場合: A(H1N1)pdm09, A(H3N2), A(H5N1) など
・N型別未実施のものが含まれる場合: A/H1pdm09, A/H3 など
・株名については, 主に国内の地名は漢字, 国外は英語表記 (例: B/山形系統, B/Victoria系統など)
・ヒトに感染したブタインフルエンザウイルスはヒトの季節性インフルエンザウイルスと区別するために, variant virusと総称し, 亜型の後に“v”を表記: A(H3N2)v など