
Isolation of Influenza Virus in Taiwan and Worldwide, 1999-2000

Introduction

Influenza virus induces local epidemics practically every year. Men and women of all ages and ethnic groups are equally affected, though young children are more susceptible. Deaths are more common among the elderly and persons of high-risk groups with complications. Entering through mouth and nostrils, the virus initially induces epidermal multiplication in the mucous membranes of the upper respiratory tract. Incubation is on average about two days, although some may develop symptoms five days after infection. Infection lasts longer in children. Typical symptoms are those of respiratory tract infection such as fever, myalgia, headache, serious malaise, coughing, sore throat, and coryza. Complications such as pneumonia may occur in young children, the elderly, and persons with chronic respiratory and cardiac problems. Without complications, recovery takes place in 7-10 days⁽¹⁾.

Influenza virus is an RNA virus of the *Orthomyxoviridae* family. It comes in types A, B and C of three different genres. Types A and B are often causes of human infection. By its two different surface antigen hemagglutinins and neuraminidase, type A can be further grouped into several subtypes. New variants of type A virus may develop as a result of antigen drift due to point mutation at the time of cloning. On the other hand, genetic

restructuring known as antigenic shift may produce viruses of new subtypes to cause worldwide pandemics. Types B and C viruses are less likely to develop variants than type A. Since 1977, H1N1 and H3N2 subtypes of influenza A viruses have induced several worldwide epidemics. Immunization of inactivated vaccine can prevent infection. However existing antibodies are not protective against antigens induced by new variants. Continual surveillance of virus variants and their seasonal variation is therefore most important.

Influenza Infection in Taiwan, 1999-2000

The laboratory surveillance system for influenza in Taiwan includes three specimen collection points in Taipei City for long term surveillance operated by the Center for Disease Control, nine contract laboratories, and 137 collection points. Specimens are collected from patients of the outpatient clinics, emergency departments or hospital wards of the medical centers of the contracted laboratories, and from the collection points in their respective responsibility regions. Throat swabs are collected from patients who meet the definition of an influenza-like illness (ILI) within three days after onset. Specimens are sent to laboratories for testing within 24 hours. Specimens are then cultured, isolated and accessed with indirect immunofluorescence assay (IFA). The isolated strains are then sent to the CDC for assay with the standard reagents supplied by the US CDC. Some representative or specific isolated strains are lyophilized and sent to the WHO Influenza Reference Laboratories in the US and Australia for further analysis⁽²⁾. Distribution of the contract laboratories is shown in Table 1.

Seasons and trends of influenza infection in Taiwan vary from north to south, they are analyzed separately to avoid any errors due to the dilution of data. Distribution of the positive rates of influenza virus during this season is shown in Figure 1. In the northern area, the number of specimens and the positive rate of influenza A began to rise in mid-November of 1999 and peaked in late December and early January 2000. In the central part of the island, as two more contracted laboratories were added in February of this year, the number of specimens was smaller, and increased significantly after March.

Positive rates in this area began to rise in late December, and remained high during January and February. In the southern part, the positive rates went up in late December to reach a peak in January. In both the northern and the southern parts of the island, at the time when the infection of influenza A declined in March, the positive rates of influenza B began to rise, and to reach another peak in late March. As compared with the infection of last year, the type A infection of this year began a month earlier.

In the northern area in the period between July 1999 and April 2000, a total of 62 type A and 14 type B virus strains were sub-typed, accounting for 22.9% of the 332 strains isolated in the entire area. Of A virus, 39 strains were of H1N1, and 23 were of H3N2. By order, more infections of H3N2 were seen prior to October 1999; whereas in the peak period of November through January 2000, more H1N1 strains were isolated. Thereafter in February, only sporadic strains were isolated. By type, 29 of the H1N1 strains were A/Beijing/262/95-like strain, and 10 were A/New Caledonia/20/99-like strain. Of the H3N2 type strains, 19 were A/Sydney/05/97-like; and two each of the A/Wuhan/359/95-like and A/Moscow/10/99-like. Type B virus had been isolated since March 2000. Assay by standard test reagent showed that they were B/Beijing/184/93-like strain.

In the central area, 14 strains of type A virus were isolated during the infection period, accounting for 36.8% of the 38 strains isolated in the entire area. Of them, 11 were H1N1, all A/Beijing/262/95-like strain; three were H3N2, all A/Sydney/05/97-like strain. In the period between July 1999 and April 2000, a total of four B strains were isolated.

In the southern area during the infection period, 15 strains of influenza virus were sub-typed, accounting for 5.8% of the 260 strains isolated in the entire area. Of them, 11 were of type A, and four were type B. Four strains of the type A virus were H1N1; of them, three were A/Beijing/262/95-like, and one was A/New Caledonia/20/99-like. Of the seven strains of H3N2, four were A/Sydney/05/95-like; two were A/Wuhan/359/95-like, and one A/Moscow/10-99-like. The four type B virus strains isolated were found to be B/Beijing/184/93-like, similar to those found in the northern area.

In general, of the virus strains isolated in the Taiwan area during the

infection season, subtypes of type B virus isolated were relatively more stable, and were similar to the subtypes isolated in 1998-1999. Subtypes of type A virus isolated were more varied as compared with the previous infection, starting with H3N2 strains prior to November 1999, to H1N1 strains after November. Of special interest is that the H1N1 virus strains isolated recently is primarily of the A/New Caledonia/20/99-like announced by the WHO to be the H1N1 type strains of the northern hemisphere in the year 2000. Some strains of the A/Moscow/10/99-like have also been isolated. This finding will serve as a basis for the selection of vaccines in Taiwan for 2000-2001.

World Trend of Influenza Infection, 1999-2000

Since October 1999, types A and B viruses have been isolated all over the world. In the Northern Hemisphere, influenza infection was still below the baseline in October and November. In November, there was a local epidemic in an area of Canada. In Europe, type A influenza infection started from southern France in early December. In the same week, Finland, Ireland and the United Kingdom had some local epidemics. From the second week of December till January 2000, influenza infections in the Northern Hemisphere had spread from a regional level to widespread level. Type A (H3N2) virus was still the main strain of the infection worldwide. Until February 2000, the infection was still active. Statistics of the WHO's FluNet showed that in the period between 1 October 1999 and 15 June 2000, a total of 35,521 strains of influenza virus had been isolated. Of them, 24,267 were of type A without any further sub-typing; 296 strains were of the A(H1N1) type; 10,463 were of the A(H3N2) type; and 494 were of type B⁽³⁾.

Countries where influenza virus was isolated during this infection season are shown in Table 2. 52 countries isolated virus of A(H3N2) type; of them, 31 are in Europe. 22 countries isolated virus of A(H1N1) type; most of them in Europe and Asia. 33 countries isolated virus of type B; of them, 15 are in Europe. There seemed to be some relatively serious outbreaks in Europe in this season. In countries close to Taiwan, mainland China, Hong Kong, Japan, the Philippines, and Singapore, both types A and B viruses were also isolated.

Subtypes of influenza virus isolated worldwide in 1999-2000 are shown in Table 3. Of type A virus, eight antigen-type strains, A/Sydney/05/97, A/Moscow/10/99, A/Panama/2007/99, A/Perugia/5/99, A/Lyon/CHU/868/99, A/Ireland/10586/99, A/Philippines/26/99, and A/Nanchang/933/95, had been isolated. Of them, A/Sydney/05/97 and A/Moscow/10/99 accounted for 80%. Four antigen-type strains of A(H1N1), A/New Caledonia/20/99, A/Johannesburg/82/96, A/Bayern/7/95, and A/Beijing/265/95, were isolated. Of them, the A/New Caledonia/20/99 strains accounted for more than a half of the total. Of type B virus, three antigen-type strains, B/Beijing/184/93, B/Yamanashi/166/98, and B/Johannesburg/5/99, were isolated. The B/Beijing/184/93 strains were the predominant. Therefore, the World Health Organization recommended the use of a composition of the A/Moscow/10/99(H3N2)-like, A/New Caledonia/20/99(H1N1)-like, and B/Beijing/184/93-like vaccines for the Northern Hemisphere in 2000-2001, and for the Southern Hemisphere in May through October 2000⁽³⁾.

Conclusion

Influenza infection in Taiwan in 1999-2000, including the subtypes of virus isolated and the period of infection, was quite different from that of the Western Hemisphere. Although there was type A infection, H1N1 was the primary strain in the peak period; it was H3N2 in the Western Hemisphere. Since the establishment of the Center for Disease Control in July 1999, a complete surveillance system for influenza has been established in collaboration with the laboratories for viral infections throughout the country to consolidate information collected through sentinel physicians and laboratories, and through close exchange with the influenza standard laboratory of the World Health Organization, to collect immediate and timely information on the trend of influenza infection. A prediction system will be developed to predict trend of infection and to give early warning. The elderly aged 65 and above are being given influenza vaccines to reduce the incidence of serious influenza infection and complications. Molecular epidemiological analysis will be strengthened to promptly understand the changes in infections, and to detect the new variants of influenza virus for early prevention and control, and thus to protect the health of the population.

Sources of Data: Division of Viral Diseases, CDC, and contracted laboratories for viral infections

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References

1. CDC. Prevention and control of influenza: Recommendations of the Advisory Committee on Immunization Practices (ACIP), MMWR 1999; 48 (No. RR-14).
2. Tseng RK, Chen HY, Hong CB. Influenza virus infections in Taiwan from 1979 to 1995. *Jan J Med Sci Biol*, 1996; 49: 77-93.
3. <http://www.who.int/emc/disease/flu>. Influenza activity during 1999-2000 season.
4. CDC. Update: influenza activity — United States and Worldwide, 1999-2000 season, and composition of the 2000-01 influenza vaccine. MMWR 2000; 49: 375-381.

Table 1 Distribution of Contracted Laboratories and their Responsibility Areas

North	National Taiwan University Hospital	(12 points in Taipei City, Keelung, Ilan,
	Chang Gung Memorial Linkou	(10 points in Taipei County, Taoyuan, and
Central	Changhua Christian Hospital	(22 points in Yunlin and Changhua)
	China Medical College Hospital	(22 points in Miaoli and Taichung City)
	Taichung Veterans' General	(15 points in Nantou and Taichung County)
South	Cheng Kung University Hospital	(14 points in Tainan City and County, and
	Kaohsiung Medical University Hospital	(11 points in Kaohisung City and County,
East	Tsu Chi Hospital	(14 points in Hualien and Taitung)
	Tri-Service General Hospital	(6 points in all military hospitals)

Table 2 Number of Countries Reported Influenza Cases

Region \ Type	A (non-type)	A(H3N2)	A(H1N1)	B
Africa	1	5	2	4
Americas	6	3	4	5
Asia	2	12	7	8
Europe	23	31	8	15
Oceania	2	1	1	1
Total	33	52	22	33

Table3 Worldwide Isolation of Influenza Viruses, 1999-2000

	Strains	No.
Type A(H3N2) virus	A/Sydney/5/97	1475
	A/Moscow/10/99	606
	A/Panama/2007/99	393
	A/Perugia/5/99	2
	A/Lyon/CHU/868/00	2
	A/Ireland/10586/99	136
	A/Philippines/26/99	3
	A/Nanchang/933/95	1
Type A(H1N1) virus	A/New Caledonia/20/99	222
	A/Johannesburg/82/96	34
	A/Bayern/7/95	53
	A/Beijing/262/95	14
Type B virus	B/Beijing/184/93	163
	B/Yamanashi/166/98	79
	B/Johannesburg/5/99	14

Figure 1. Influenza Virus Positive Rates by Region, Taiwan



