SEASONAL INFLUENZA VIRUS STRAINS CIRCULATING IN MALAYSIA FROM 2005 TO 2009

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Abstract. From 2005 to 2009, the Institute for Medical Research (IMR), Kuala Lumpur received a total of 7,117 respiratory specimens from patients with influenza-like illness (ILI) for influenza screening. Seasonal influenza virus was isolated from 17.3% of patients with ILI in 2005, 31.6% in 2006, 12.8% in 2007, 10.2% in 2008 and 13.5% in 2009. There were one or more influenza A and B virus strains circulating in Malaysia throughout the year, with distinctly a peak in May to August. The predominant circulating strains of seasonal influenza A were A/California/7/2004-like (H3N2) in 2005, A/New Caledonia/20/99-like (H1N1) in 2006, A/Brisbane/10/2007-like (H3N2) in 2007 and 2008, and A/Perth/16/2009-like (H3N2) virus in 2009. The predominant circulating strains of influenza B were B/Hong Kong/330/2001-like in 2005, B/Malaysia/2506/2004-like in 2006, B/Florida/4/2006-like in 2007 and 2008, and B/Brisbane/60/2008-like in 2009.

Key words: influenza virus, circulating strain, Malaysia

INTRODUCTION

Influenza viruses are permanently evolving, thus, an epidemic of influenza occurs almost every year. These epidemics are thought to result in 3 to 5 million cases of severe illness and 250,000 and 500,000 deaths each year worldwide (WHO, 2009). Influenza had adversely affected the health and economics of the global population during three pandemics in the 20th century as well as during seasonal epidemics.

The World Health Organization (WHO) global influenza surveillance network was set-up in 1952 as a worldwide alert system for the identification of new influenza viruses with pandemic potential. To date, the network is comprised of 5 WHO Collaborating Centers (WHO CCs), 4 Essential Regulatory Laboratories and 131 institutes from 102 countries as National Influenza Centers (NICs). The CCs perform high level antigen and genetic analyses of isolates received from NICs as a basis for WHO recommendations on the composition of influenza vaccines for the northern and southern hemispheres each year (WHO, 2010). Influenza vaccine content needs to be updated frequently since influenza viruses are continuously evolving. Only a vaccine whose virus strains match the circulating influenza viruses will protect recipients from influenza

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infections and death.

Influenza surveillance in Malaysia was first established in 1954 and in 1968 the Virology Unit, Institute for Medical Research (IMR), Kuala Lumpur was designated as one of the National Influenza Centers (NIC) for Malaysia. Since then, the Virology Unit has continued to carry out influenza surveillance activities for the Ministry of Health (MOH) Malaysia, involving participating government hospitals and outpatient clinics throughout the country as sentinel sites. Like other countries, the types and proportions of influenza type A and influenza type B viruses circulating vary each year in Malaysia. During the past five years, several outbreaks of influenza A and B have been reported in this country.

The national influenza surveillance program in Malaysia plays an important role in preparing for, and responding to epidemics and pandemics. Currently, based on surveillance data, the vaccine recommended for the southern hemisphere is being used in Malaysia. This study aims to evaluate the annual incidence and identify the strains of influenza virus circulating in this country from 2005 until 2009.

MATERIALS AND METHODS

Between January 2005 and December 2009 all respiratory specimens received at the NIC, IMR, from patients presenting with influenza-like illness (ILI) were screened for seasonal influenza viruses. Specimens received for pandemic influenza A (H1N1) 2009 were not included in this study.

Specimens were inoculated into Madin-Darby Canine Kidney (MDCK) cells and isolates were identified by the indirect imunofluorescence antibody technique (IFAT) using specific monoclonal antibodies against influenza types A and B (Light Diagnostics, Cat. no. 3105). The influenza isolates were typed and subtyped by hemagglutination inhibition (HAI) assays as described by Lennette and Schmidt (1979); using human group O+ blood, reference antisera and antigen controls provided by the WHO Collaborating Center, Melbourne. Identification of the field isolate was carried out by comparing the results of the unknown isolate with those of the antigen control. An isolate was identified as a specific influenza A subtype if the subtype-specific HAI titer was fourfold or greater than the titer obtained with the other antiserum. The WHO Manual on Animal Influenza Diagnosis and Surveillance (2002) was followed.

Following the type and subtype identification of influenza A, the influenza isolates were sent to the WHO Collaborating Center for Reference and Research on Influenza in Melbourne, Australia for strain identification (by HAI assay) and further analysis.

RESULTS

From 2005 to 2009, the NIC, IMR received a total of 7,117 respiratory specimens from patients with influenza-like illness (ILI), of which 14.0% (993/7,117) were positive for influenza virus. Seasonal influenza virus was isolated from 17.3% (160/923) of patients with ILI in 2005, 31.6% (145/459) in 2006, 12.8% (236/1,847) in 2007, 10.2% (225/2,210) in 2008 and 13.5% (227/1,678) in 2009 (Fig 1).

Of the 993 positive cases, 69.3% (688/993) were influenza A and 30.7% (305/993) were influenza B. Except for 2005, influenza type A virus was isolated more often than influenza type B virus (Fig 2). In 2005, 51.3% (82/160) of the influenza positive

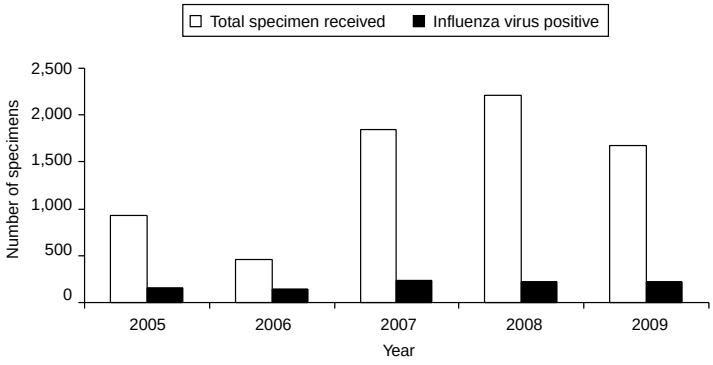

Fig 1–Total clinical specimens received for ILI surveillance from 2005 to 2009.

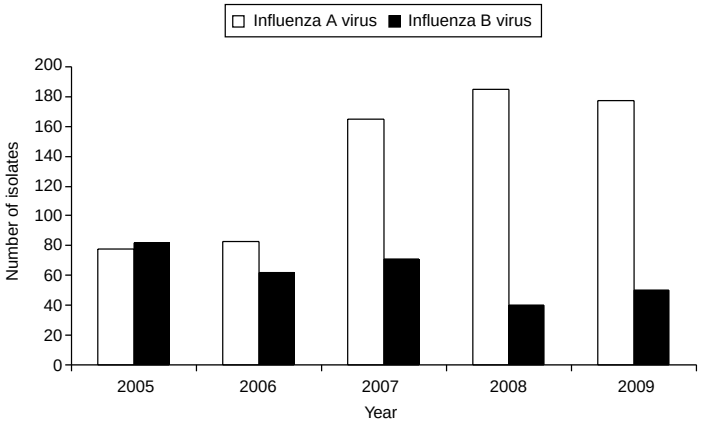

Fig 2–Influenza A and B viruses isolated from samples for ILI surveillance from 2005 to 2009.

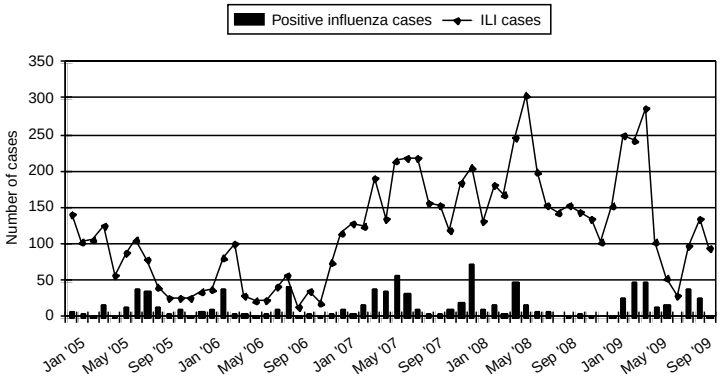

Fig 3–Distribution of ILI cases and influenza virus positive cases during 2004 to 2009.

samples were influenza type B and 48.7% (78/160) were influenza type A. Fifty-seven point two percent (83/145) of positive samples were influenza type A and 42.8% (62/145) were influenza type B in 2006; 69.9% (165/236) influenza A and 30.1% (71/236) influenza B in 2007; 82.2% (185/225) influenza A and 17.8% (40/225) influenza B in 2008; and 78.0% (177/227) influenza A and 22.0% (50/227) influenza B in 2009.

During the past 5 years, ILI occured all year round in Malaysia with a peak in May to August (Fig 3). The highest influenza virus isolation rate occurred in July to August (47.5%, 76/160) in 2005, March (28.3%, 41/145) and September (29.0%, 42/145) in 2006, May to August (69.9%, 165/236) in 2007, February (32.9%, 74/225) and June to August (34.7%, 78/225) in 2008; and May to June (42.7%, 97/227) in 2009.

Since the southern hemisphere influenza vaccine is used in Malaysia, only southern hemisphere vaccine formulation strains were used to compare with circulating viruses during this surveillance study. Table 1 shows the percentage of influenza A virus strains circulating in Malaysia from 2005 to 2009 versus the southern hemisphere vaccine formulation strains. The predominant circulating influenza A strains

Table 1
Predominant influenza type A virus strains circulating in Malaysia from 2005 to 2009.

Year	Circulating influenza type A virus strains	%	WHO vaccine component (southern hemisphere)
2005	A/California/7/2004-like (H3N2) virus	62.0	A/New Caledonia/20/99(H1N1)-like virus
	A/New Caledonia/20/99-like (H1N1) virus	25.3	A/Wellington/1/2004(H3N2)-like virus
	A/Wellington/1/2004-like (H3N2) virus	12.7	
2006	A/New Caledonia/20/99-like (H1N1) virus	57.9	A/New Caledonia/20/99(H1N1)-like virus
	A/Wisconsin/67/2005-like (H3N2)	42.1	A/California/7/2004(H3N2)-like
2007	A/Brisbane/10/2007-like (H3N2) virus	40.0	A/New Caledonia/20/99(H1N1)-like virus
	A/Solomon Island/3/06-like (H1N1) virus	36.4	A/Wisconsin/67/2005(H3N2)-like virus
	A/Wisconsin/67/2005-like (H3N2) virus	24.6	
2008	A/Brisbane/10/2007-like (H3N2) virus	90.0	A/Solomon Islands/3/2006 (H1N1)-like virus
	A/Brisbane/59/2007-like (H1N1) virus	10.0	A/Brisbane/10/2007 (H3N2)-like
2009	A/Perth/16/2009-like (H3N2) virus	73.8	A/Brisbane/59/2007 (H1N1)-like virus
	A/Brisbane/10/2007-like (H3N2) virus	26.2	A/Brisbane/10/2007 (H3N2)-like virus

Table 2
Percentage of predominant influenza type B virus strains circulating in Malaysia from 2005 to 2009.

Year	Circulating influenza type B virus strains	%	WHO vaccine component (southern hemisphere)
2005	B/Hong Kong/330/2001-like virus[a]	79.0	B/Shanghai/361/2002-like virus[b]
	B/Malaysia/2506/2004-like virus[a]	19.8	
	B/Shanghai/361/2002-like virus[b]	1.2	
2006	B/Malaysia/2506/2004-like virus[a]	94.2	B/Malaysia/2506/2004-like virus[a]
	B/Shanghai/361/2002-like virus[b]	5.8	
2007	B/Florida/4/2006-like virus[b]	44.1	B/Malaysia/2506/2004-like virus[a]
	B/Shanghai/361/2002-like virus[b]	28.8	
	B/Malaysia/2506/2004-like virus[a]	27.1	
2008	B/Florida/4/2006-like virus[b]	100.0	B/Florida/4/2006-like virus[b]
2009	B/Brisbane/60/2008-like virus[a]	67.6	B/Florida/4/2006-like virus[b]
	B/Malaysia/2506/2004-like virus[a]	29.7	
	B/Florida/4/2006-like virus[b]	2.7	

[a] B/Victoria lineage virus; [b] B/Yamagata lineage virus

were A/California/7/2004-like (H3N2) in 2005, A/New Caledonia/20/99-like (H1N1) in 2006, A/Brisbane/10/2007-like (H3N2) in 2007 and 2008; and A/Perth/16/2009-like (H3N2) virus in 2009.

Table 2 shows the percentage of the predominant influenza type B virus strains circulating in Malaysia from 2005 to 2009 compared to the southern hemisphere vaccine formulation strains. The predominant

circulating influenza B strains were B/ Hong Kong/330/2001-like in 2005, B/Malaysia/2506/2004-like in 2006, B/Florida/4/ 2006-like in 2007 and 2008 and B/Brisbane/ 60/2008-like in 2009.

DISCUSSION

Malaysia Influenza Surveillance System (MISS) is comprised of both ILI sentinel surveillance and influenza viral surveillance. Presently, ILI data are collected from 216 sentinel sites which consist of outpatient departments of government health clinics.

The positive isolation rate for influenza virus among the clinical specimens was low for both influenza A and B viruses isolated during the surveillance period in Malaysia. A reason for the low isolation rate could by the loss of viability of the virus during transportation of specimens. Over seven percent (518/7,117) of specimens were received at ambient temperature and >35% (2,498/7,117) of specimens arrived in the laboratory more than 4 days after they were collected.

In Malaysia, influenza seasonality is less defined than in temperate countries. Shahidah *et al* (2003) reported influenza occurred all year round with a peak during the dry season from April to June, and during the wet season from October to January. This bimodal peak was not seen during the past five years. In 2005 to 2009, influenza viruses were most commonly isolated during May to August.

Two to 3 types of influenza A virus were seen circulating simultaneously each year (Table 1). The influenza A (H1N1) strains circulating in Malaysia in 2005 and 2006 were compatible with the strain used in the WHO 2005 and 2006 southern hemisphere vaccine. However, the H1N1 vaccine strains were not a perfect match for the years 2007 and 2008. The influenza A (H3N2), virus strains used for the WHO 2007, 2008 and 2009 vaccines were compatible with the H3N2 strains circulating in Malaysia during the same time period.

The influenza B viruses circulating can be divided into two distinct lineages represented by the B/Yamagata/16/88 and B/ Victoria/02/87 viruses; these were among the 3 strains circulating each year in Malaysia (Table 2).

In late 2004, the B/ Malaysia/2506/ 2004-like virus evolved from the B/ Victoria-lineage and was isolated in 19.8% of influenza positive cases in Malaysia in 2005 and then became the predominant circulating strain in Malaysia in 2006. The predominant circulating influenza type B virus strains for 2006 and 2008 were compatible with the strains in the southern hemisphere vaccine. However, the vaccines for 2005, 2007 and 2009 were not compatible with the predominant influenza B virus strains circulating during those years.

During 2005, several small outbreaks occurred in the community. These outbreaks were reported in institutions, such as boarding schools and national service camps, not under the current surveillance system. The current system failed to detect outbreaks of ILI in the community. There is a need to improve the ILI sentinel surveillance and flu-viral surveillance systems in Malaysia to better detect early outbreaks and monitor circulating influenza viruses in the community.

In Malaysia, influenza viruses were found to circulate throughout the year with higher occurrences during the middle part of the year. There are usually 3 to 6 influenza virus strains co-circulating simultaneously each year. The annual WHO recommendations for influenza vaccine

components are based on antigenic and genetic analysis of recent influenza virus isolates worldwide. Surveillance activities are important to ensure a good match between vaccine strains and actual circulating strains. This study emphasizes the importance of a local influenza surveillance program not only as an early warning of upcoming epidemics but to develop appropriate annual influenza vaccines.

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