

HIGHER THAN EXPECTED SEASONAL INFLUENZA ACTIVITY IN VICTORIA, 2007

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Abstract

In 2007, the Victorian influenza season exceeded normal seasonal activity thresholds. The average rate of influenza-like illness (ILI) reported by general practitioners (GPs) participating in sentinel surveillance was 9.0 cases per 1,000 consultations, peaking at 22 cases per 1,000 consultations in mid-August. The average ILI rate reported by the Melbourne Medical Locum Service (MMLS) was 11.5 per 1,000 consultations over the season. The MMLS ILI rate peaked at 30 per 1,000 consultations at the same time as peak rates were reported by GPs, with a secondary peak observed three weeks later (22 cases per 1,000 consultations). Influenza cases notified to the Victorian Department of Human Services peaked in mid-August with a secondary peak of influenza A in early September. Of the influenza positive swabs collected by GPs and among those collected throughout the state, 92% were type A and 8% were type B. The most common strains identified in Victoria in the 2007 influenza season were A/Brisbane/10/2007-like followed by A/Solomon Islands/3/2006-like. While neither virus strain was specifically included in the 2007 Australian influenza vaccine, reasonable cross protection was afforded by the strains in the vaccine. *Commun Dis Intell* 2008;32:63–70.

Keywords: surveillance, epidemiology, influenza

Introduction

A sentinel general practice (GP) program for the surveillance of influenza like illness (ILI) has been conducted in Victoria since 1993. Laboratory testing for cases meeting selection criteria was introduced to the GP sentinel system in 1998.¹ The Victorian Infectious Diseases Reference Laboratory (VIDRL) also monitors diagnoses of ILI made by GPs in the Melbourne Medical Locum Service (MMLS). Under the *Health (Infectious Disease) Regulations 2001*,² the Department of Human Services (DHS) coordinates the surveillance of laboratory notifications of influenza. These three elements (sentinel GP surveillance, MMLS monitoring and DHS surveillance) constitute the Victorian Influenza Surveillance System.

Supplementing the Victorian Influenza Surveillance System, the World Health Organization (WHO) Collaborating Centre for Reference and Research

on Influenza (also based in Melbourne) undertakes strain typing of influenza isolates and influenza specimens identified through the GP sentinel surveillance programs as well as those forwarded by two Melbourne hospital-based laboratories.

The Victorian influenza surveillance system aims to:

- monitor the occurrence of laboratory-confirmed influenza in Victoria;
- describe the epidemiology of influenza in Victoria – identifying the onset, duration and magnitude of each influenza season; and
- characterise the strains of influenza in the community to assist in monitoring the impact of the current vaccine and the formulation of vaccines for the subsequent season.

In this paper we summarise findings from the Victorian Influenza Surveillance System in 2007.

Methods

General practice sentinel surveillance

Participating GPs were asked to report weekly on the total number of consultations they had for the week, and the age, sex and vaccination status of any patients presenting with ILI. In line with accepted case criteria, ILI was defined as history of fever, cough and fatigue/malaise.³ Nose and throat swabs were offered to patients presenting within three days of the onset of their symptoms. Once formal consent was obtained from these patients, GPs collected data on their age, sex, symptoms (fever, cough, fatigue, myalgia, other) and vaccination status. GPs were also asked to provide an indication of their confidence in their clinical diagnosis of influenza ('almost certain,' 'probable' or 'less likely'). Registered as approved activities by the Royal Australian College of General Practitioners and the Australian College of Rural and Remote Medicine, GPs were offered Continuing Professional Development for their participation in the program.

Swabs were transported to VIDRL by courier where they were tested using an in-house respiratory multiplex polymerase chain reaction (PCR) test identifying influenza, adenovirus, picornavirus (enterovirus and rhinovirus), respiratory syncytial virus and parainfluenza viruses.

A development of a previous assay,⁴ the current test uses type specific primers that identify influenza B and all influenza A sub-types.

Data for the 22-week period 30 April to 30 September 2007 were analysed using the set of threshold values previously established for Victorian influenza seasons.⁵ Rates of ILI cases per 1,000 consultations for baseline activity, normal seasonality and higher than expected activity were defined as below 2.5, between 2.5 and <15, and between 15 and <35 respectively. According to these thresholds, 'epidemic influenza activity' is defined by rates exceeding 35 cases per 1,000 consultations.

The recommendation of the *Framework for an Australian Influenza Pandemic Plan* (1999)⁶ was for sentinel surveillance to achieve recruitment coverage of approximately one practice per 200,000 in metropolitan areas and one practice per 100,000 population in rural areas. These recommendations, however, do not take into account the number of GPs participating in each practice or the fraction of time each GP spends consulting. We have previously suggested that a relatively small number of practices with better response rates is able to provide data on seasonal influenza activity that

are as useful as those provided by a larger number of practices with poorer participation.⁷ We demonstrated that the number of GP consultations per population in a given region better measured geographic representation than the number of practices per population, and we proposed that a small number of 'dedicated' participating sites seeing around 2,000 consultations per 100,000 population over the influenza season should be used as the recruiting target.

In 2007 there were 50 GPs participating in 15 metropolitan practices and 15 GPs participating in six rural practices. The geographical locations of recruited practices are presented in Figures 1a and 1b.

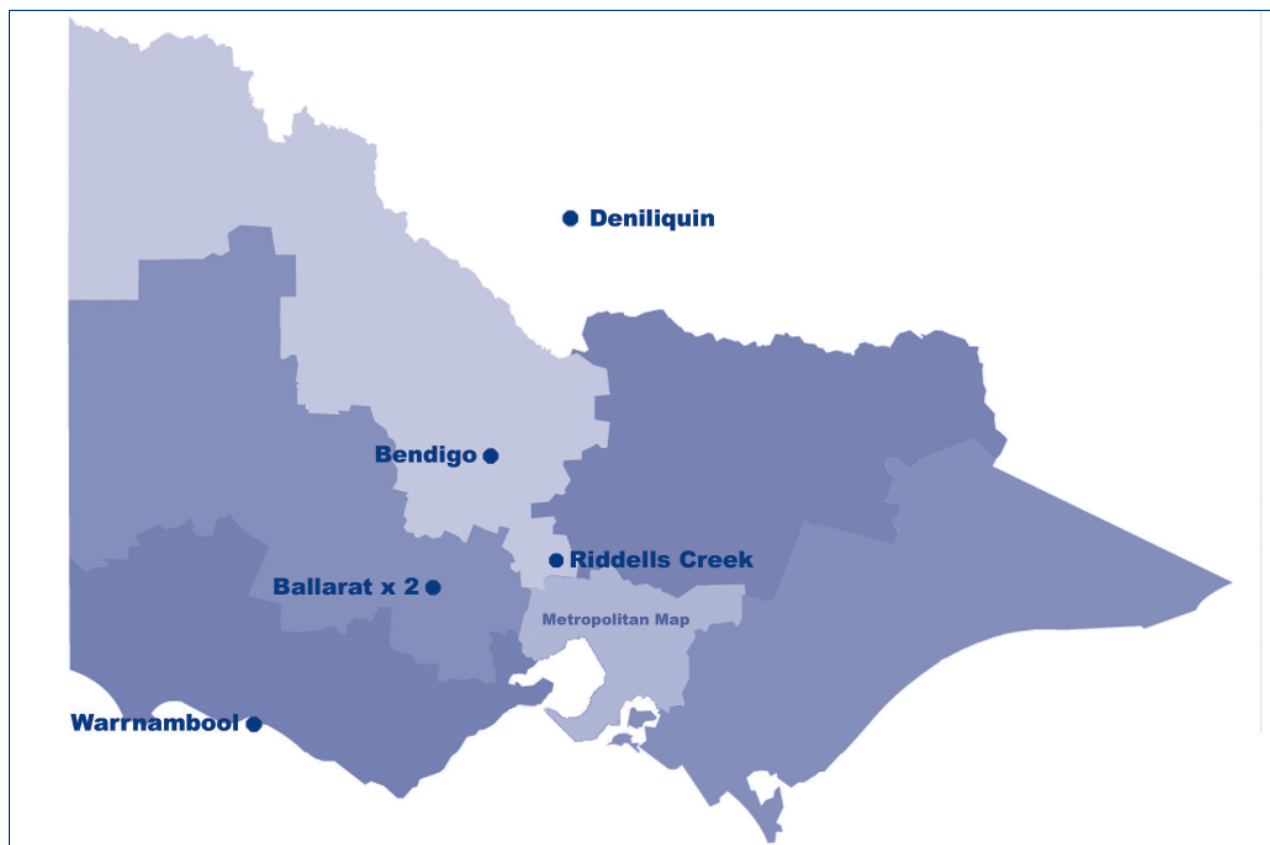
Melbourne Medical Locum Service

The largest medical locum service in Australia, the Melbourne Medical Locum Service operates a 24-hour service throughout metropolitan Melbourne each day. Weekly searches of the clinical database maintained by the MMLS, using the search terms 'influenza' or 'flu,' provides data on the number of influenza-related diagnoses made by MMLS GPs. These data and the total number of consultations made by the MMLS are available from the password protected MMLS website.

Figure 1a. Distribution of sentinel surveillance sites in metropolitan Victoria 2007



Figure 1b. Distribution of sentinel surveillance sites in rural Victoria 2007



Notified laboratory-confirmed influenza

Under the *Health (Infectious Diseases) Regulations 2001*,² medical practitioners and pathology services are required to notify confirmed influenza cases to the DHS within five days of the positive test. Data on cases notified during the surveillance period were identified in the DHS Notifiable Infectious Disease Surveillance database and extracted for analysis on 22 October 2007.

Data collation and reporting

As well as requesting laboratory tests, GPs reported ILI cases to VIDRL by facsimile, each week. Data on influenza related diagnoses were extracted from the MMLS database each week. Weekly information was reported to the DHS Communicable Disease Control Unit and to the Australian Government Department of Health and Ageing. Every two weeks, structured reports on the previous fortnight were distributed to all participating GPs, state and Australian health departments and other interested health professionals and health agencies, and were also made available on the VIDRL web site (at <http://www.vidrl.org.au>). Summary reports of (laboratory-confirmed) influenza notifications were updated daily and posted on the DHS Communicable Disease Control Unit web site (<http://www.health.vic.gov.au/ideas/surveillance/daily.htm>).

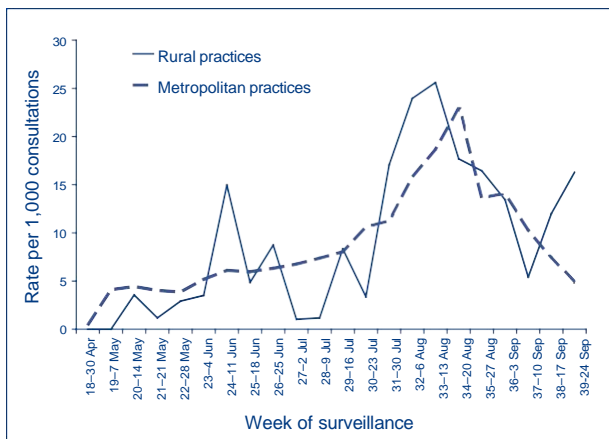
Results

ILI surveillance

Across the 22 weeks of surveillance, an average of 95% (61/65) of GPs returned tally sheets to VIDRL each week (range 86% to 98%). GPs reported having conducted 115,646 consultations and identified 1,045 ILI cases during the season – an overall rate of 9.0 per 1,000 consultations. From a baseline rate averaging around 3.0 cases per 1,000 consultations in the first weeks of surveillance, the rate peaked in mid-August (week beginning 20 August) at 21.9 cases per 1,000 consultations, before declining to 7.1 ILI cases per 1,000 consultations at the end of the surveillance period – over two times the baseline rate. There appeared to be a differential metro–rural pattern of disease in 2007 (Figure 2). The rural peak (25.6 ILI cases per 1,000 consultations) occurred a week earlier than the metropolitan peak, and declined less steeply before a secondary peak was reported at the end of the surveillance period, or the last week in September (16.4 ILI cases per 1,000 consultations). In 2007, overall ILI rates reported by GPs did not return to baseline until mid-October (data not shown).

Among the total ILI cases reported by GPs, 55% (572/1,045) were female and 45% (472/1,045) were male. The median age of ILI cases was 32 years

Figure 2. Weekly influenza-like illness rates reported, Victoria, 2007, by rural and metropolitan practices



(range one to 95 years) and 82% (854/1,045) were reported as being unvaccinated for the season. Among the cases aged 65 years or older, 16% (11/69) were unvaccinated.

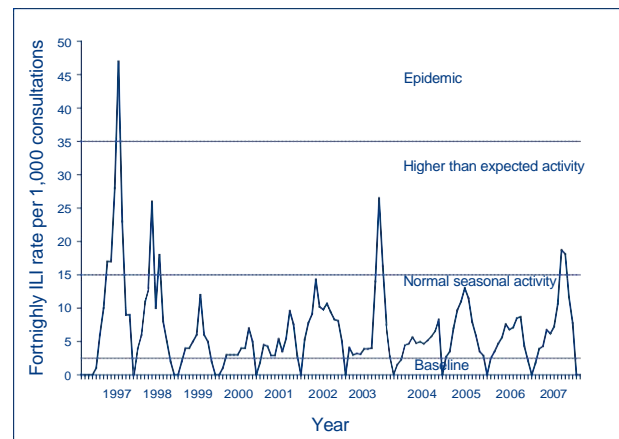
Among consultations conducted by the MMLS during the 2007 season, 362 patients were diagnosed with 'flu' or 'influenza.' The average ILI rate in 2007 reported by the MMLS was 11.5 cases per 1,000 consultations. ILI rates followed a similar pattern to that reported by rural GPs with a peak over two weeks in mid-August (30.0 ILI cases per 1,000 consultations) and a secondary peak in mid-September (21.4 ILI cases per 1,000 consultations). By the final week of the surveillance period the ILI rate per 1,000 consultations had declined to 8.4, but did not return to baseline until mid-October (data not shown).

Using the previously described thresholds for GP sentinel surveillance in Victoria, ILI rates in 2007 exceeded those of the previous three seasons and, for the first time since 2003, were in the range of 'higher than expected activity' (Figure 3). The peak was not as high as earlier seasons in which higher than expected activity was reported (i.e. 1997, 1998 and 2003).

Laboratory surveillance

Participating GPs submitted a total of 403 patient swabs to VIDRL, with a median of five swabs submitted per GP (range one to 24 swabs). Overall, 62% (248/403) of the total swabs tested positive to any of the respiratory viruses forming part of the multiplex PCR. As can be seen in Table 1, 67% (165/248) of those testing positive for respiratory viruses were positive for influenza A and 10% (24/248) were influenza B positive (including two swabs positive for both influenza A and B). Over 80% of influenza diagnoses were made between weeks 29 to

Figure 3. Fortnightly GP sentinel surveillance influenza-like illness rates, Victoria, seasons 1997 to 2007



36 (16 July to 9 September). Approximately 17% (43/165) of the swabs tested positive for picornavirus, the diagnoses of which were distributed relatively equally throughout the surveillance period. The overall positive predictive value (PPV) for all clinical diagnoses of influenza made by all GPs was 47% (the median for individual GPs was 33%). PPV rose with the certainty of the diagnosis, with those reporting they were 'almost certain' of their clinical diagnosis achieving an overall positive predictive value of 64% (individual GP median 69%). PPV for the years 2002 to 2007 are presented in Table 2. Although not apparent in the 2003 season, also a year of above expected activity, PPVs can ordinarily be expected to increase with increasing prevalence of influenza in the population.⁸

Among those testing positive for influenza A or B, 45% (83/185) of the specimens were provided by female patients and 55% (102/185) by male patients. The median age of these patients was 27 years (range 0 to 92 years) and 70% (128/183) reported being unvaccinated for the 2007 season, 11% (21/183) reported being vaccinated and 19% (34/183) had unknown vaccination status.

VIDRL provided approximately 55% of all notifications to DHS during the surveillance period, with 12 other Victorian laboratories providing notifications for approximately 51% of cases; the sum of the percentages is greater than 100% because some cases were tested and notified by multiple laboratories. During the surveillance period, a total of 1,343 laboratory-confirmed cases of influenza were notified to the DHS, representing a 256% increase on the numbers notified during the 2006 surveillance period (377 cases). Approximately 15% of this total included the laboratory-confirmed cases identified through GP sentinel surveillance, and around 8% were identified during outbreak investigations. Around 54% (723/1,343) of the notifications were in

Table 1. Respiratory viruses detected from general practice sentinel surveillance influenza-like illness patient swabs, 2007

Respiratory virus	n detected	% detected (total swabs)	% detected (PCR positive swabs)
Influenza A	165	41	67
Influenza B	24	6	10
Picornavirus	43	11	17
Adenovirus	4	1	2
Parainfluenza virus	4	1	2
Respiratory syncytial virus	8	2	3
Total	248	62	100

Table 2. Positive predictive value of clinical diagnoses of influenza, 2002 to 2007, by general practitioner certainty of diagnosis

Year of surveillance	General practice certainty of diagnosis – number laboratory confirmed (PPV)									
	Almost certain		Probable		Less likely		Not stated		Total	
	n	PPV%	n	PPV%	n	PPV%	n	PPV%	n	PPV%
2002	25	45	94	35	23	24	25	45	167	38
2003	87	45	73	29	4	9	20	38	184	34
2004	12	26	23	16	6	13	2	9	43	16
2005	74	61	90	41	8	15	10	43	182	43
2006	48	51	56	27	11	21	11	41	126	33
2007	85	64	91	44	5	13	8	38	189	47

females and 46% (611/1,343) were in males (sex was not reported in nine cases) and the median age was 31 years (range 0 to 97 years).

The majority of the DHS notifications—nearly 77%—resulted from clinical presentations not forming part of the surveillance system. Of the total cases, 86% (1156/1343) were influenza A, 14% (186/1,343) were influenza B and one case was notified with both influenza A and B. As can be seen in Figure 4, the number of notified influenza A cases increased in line with the MMLS and GP surveillance ILI rates, with a peak in mid-August (weeks 33 and 34). A secondary peak of influenza A occurred in early September (week 36), one week prior to the secondary peak in ILI cases diagnoses reported by the MMLS. Notifications for influenza B, which made up 16% of all influenza notifications in 2007, had a later peak in mid-September (weeks 37 and 38), which was preceded by a smaller peak in mid-August (week 34). A further peak in DHS notifications of laboratory-confirmed cases of influenza B occurred after the end of the surveillance period, in late October to early December (data not shown).

Figure 5 presents laboratory-confirmed influenza A and B are stratified according to source of identification. Broadly reminiscent of the bimodal presentation of DHS notifications, influenza A cases

identified by the GP surveillance program peaked a week earlier than the DHS influenza A cases and plateaued two weeks ahead of the secondary DHS influenza A peak. The number of influenza B cases identified by GPs was too small to identify trends over time.

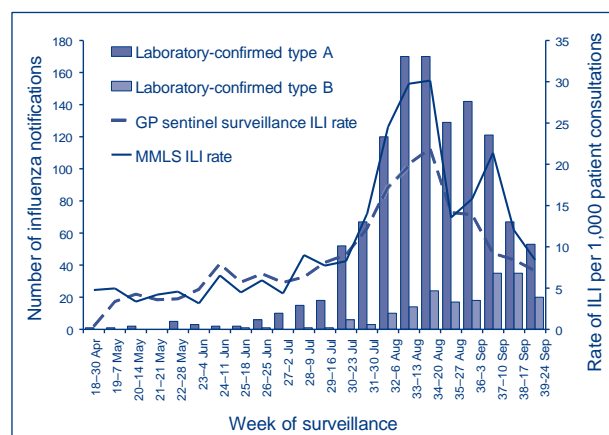
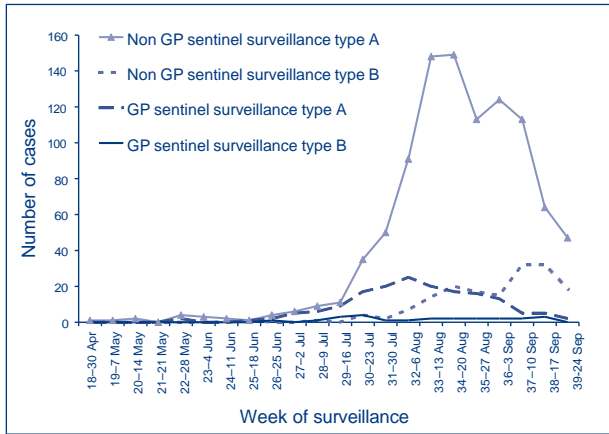
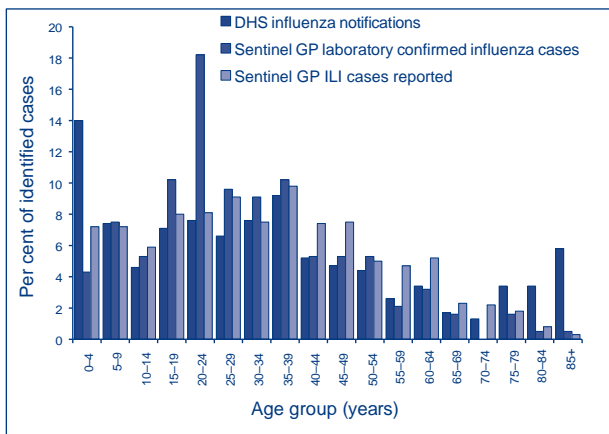
Figure 4. Notified cases of laboratory-confirmed influenza and general practitioner sentinel surveillance and Melbourne Medical Locum Service influenza-like illness rates, Victoria, 30 April to 27 September 2007, by week

Figure 5. Laboratory-confirmed influenza, Victoria, 30 April to 27 September 2007, by type and notification source



The relative age distributions of cases according to notification source, DHS and GP sentinel surveillance (ILI cases and laboratory-confirmed cases) are presented in Figure 6. There were differences in the age distributions from the two surveillance sources. Around 14% (188/1,343) of the DHS notifications were in cases aged under five years, compared to 4% (8/187) of GP laboratory-confirmed cases and 7% (65/902) of ILI cases reported by GPs. Those aged 75 years or older made up 12% (168/1,343) of DHS notifications but only 3% of GP laboratory-confirmed cases (5/187) and GP reported ILI cases (26/902). GP laboratory-confirmed cases were most prevalent in those aged 20 to 24 years, who made up 18% (35/187) of cases from this source. In contrast, 8% of both DHS notifications (102/1,343) and GP ILI cases (73/902) were in the 20 to 24 year age group. Two cases among those notified during the surveillance period were reported to have died as a result of type A influenza virus infection: an 84-year-old

Figure 6. Laboratory-confirmed influenza and influenza-like illness cases, Victoria, 30 April to 27 September 2007, by proportion of age group and notification source



female and a 91-year-old male. A further five cases aged five years and between 68 and 90 years were reported to have died with a type A influenza virus infection, but death was attributed to other causes.

A total of 105 isolates and 224 specimens collected in Victoria were referred to the WHO Collaborating Centre for Reference and Research on Influenza. Of these, 187 specimens (57%) were collected through GP sentinel surveillance. At time of writing, data were available from 170 of the influenza positive specimens sent (149 were influenza A, 21 influenza B). Only 24% (40/170) of specimens (mostly collected through the sentinel surveillance) yielded recoverable isolates. Of the 34 influenza A isolates, 56% (19/34) were A/Solomon Islands/3/2006-like (H1) and 29% (10/34) were A/Wisconsin/67/2005-like (H3) and (5/34) 15% were A/Brisbane/10/2007-like (H3). Three of the six influenza B samples were B/Malaysia/2506/2004-like, two were B/Shanghai/361/2002-like and one was B/Florida/4/2006-like.

Among the 329 specimens and isolates collected throughout Victoria during 2007 and referred to the WHO Centre, 50% (165/329) were recoverable of which 90% (148/165) were type A and 10% (17/165) were type B. Thirty-seven per cent (55/148) of the type A isolates were further characterised as H1N1 strains comprised of: A/Solomon Islands/3/2006-like (96%, including nine low reactors); and A/New Caledonia/20/99-like (4%). Approximately 63% (93/148) of the remaining influenza A isolates were H3N2 strains comprised of: A/Brisbane/10/2007-like (58%, including nine low reactors); and A/Wisconsin/67/2005-like [42%, most of which (30/39) were low reactors]. The 17 influenza type B isolates were designated as B/Florida/4/2006-like, 41% (7/17) and B/Shanghai/361/2002-like (low reactor), 35% (6/17) – giving a total of 76% B/Yamagata/16/88-like lineage virus. The remaining 24% (4/17) were B/Malaysia/2506/2004-like (low reactor), being of the B/Victoria/2/87-like lineage.

The Australian influenza vaccine for 2007 contained A/New Caledonia/20/99, A/Wisconsin/67/2005 and B/Malaysia/2506/67/2004 strains.⁹

Outbreak investigations

The Communicable Disease Control Unit (DHS) investigated 24 respiratory outbreaks during the reporting period, of which 16 were confirmed as due to type A influenza virus, one was due to type B influenza virus, three were due to respiratory syncytial virus and a cause was unable to be established for four outbreaks. With the exceptions of a defence facility and rehabilitation centre, all notified influenza outbreaks occurred in aged care settings. Outbreaks occurred in aged care facilities, which accommodated between 24 and 107 residents, with

attack rates among residents ranging from 9% to 46%. These outbreaks were investigated and appropriate control measures implemented in accordance with the *Guidelines for the Control of Respiratory Disease Outbreaks in Aged Care Facilities in Victoria*.

Discussion

Across Australia, more influenza cases were notified in 2007 relative to the past few years. The 2007 year-to-date national laboratory-confirmed notifications to the end of October were increased by close to 240% on the previous year and were 3.4 times the five-year mean number of notifications.¹⁰ Consistent with the national influenza season, Victoria experienced a 270% increase in notifications this year compared with the same period in 2006 and ILI rates from GP sentinel surveillance were in the range of 'higher than expected activity.' While higher than at any time since 2003, the ILI rate was below that experienced in 2003 and considerably lower than during the influenza epidemic of 1997. The importance of historical threshold data in evaluating the relative severity of seasons is clearly demonstrated by these figures. While notification numbers were increased in Victoria in line with the national increase, threshold analysis indicated that the 2007 season was no worse than the 2003 season.

Regardless of the source of notification, the Victorian influenza season was characterised by a bimodal frequency distribution over time; reaching peak activity in mid-August in 2007. A secondary peak in early September was observed in notification data, in mid-September in MMLS data and in late September in the rural component of GP sentinel surveillance.

As has been noted in previous years, population age-structure varies according to reporting source. The DHS notifications contained a large proportion of notifications of laboratory-confirmed influenza in children below five years of age, as well as a relatively large proportion of notifications in elderly patients. This is largely because these notifications are predominantly made from hospitals, with these age groups most at risk of hospitalisation. In contrast, those aged between 20 and 24 years were the largest group with laboratory-confirmed influenza presenting with ILI to sentinel surveillance GPs. The age structure for non-laboratory-confirmed ILI cases reported by sentinel surveillance GPs, however, was more symmetrically distributed. The increased proportion of positive swabs from young adults, which also featured in previous years of GP sentinel surveillance, may be due to several factors. For instance, workplace or university requirements for sick certificates may increase the number of patients in this age group presenting to the GP within the first three days of symptoms appearing (one of the defined case criteria for swabbing). Although this

was not reported by participating GPs, there may be greater compliance with the swabbing procedure in this age group.

The influenza typing and strain data available for Victoria suggest that the pattern of approximately 90% type A and 10% type B was distributed relatively evenly over the season. The Australian influenza vaccine for 2007 contained A/New Caledonia/20/99-like, A/Wisconsin/67/2005-like and B/Malaysia/2506/67/2004-like strains.⁹ The most commonly isolated strains of influenza A were A/Solomon Islands/3/2006-like A(H1) and A/Brisbane/10/2007-like A(H3) strains, while B/Florida/4/2006 and B/Shanghai/361/2002-like strains were the most commonly isolated influenza B strains in Victoria. Both the influenza A(H1) and A(H3) strains most commonly circulating in Victoria in 2007 represented drift variants from the virus contained in the 2007 vaccines. While these viruses can be distinguished antigenically using specific ferret sera or by molecular sequencing of the haemagglutinin gene, a reasonable level of cross reactivity between vaccine and circulating influenza A strains would be expected for the influenza A viruses.

For the influenza B viruses, the most commonly circulating viruses were of the B/Yamagata/16/88-lineage (B/Florida/4/2006 and B/Shanghai/361/2002-like viruses) while the minority were similar to the 2007 vaccine strain, B/Malaysia/2506/2004. While there is some measurable cross reactivity generated with one B-lineage against the other, higher levels of immunity would be expected against viruses of the same lineage. As it is currently only possible to have one influenza B-lineage in the influenza vaccine, it is not possible to have a perfect match while both the influenza B-lineages are co-circulating.

The GP sentinel program continues to enhance Victoria's overall influenza surveillance effort by contributing additional information not easily obtained through passive surveillance systems. In 2007, the GP surveillance period was extended in order to accommodate the piloting of GP surveillance for varicella-zoster virus (chickenpox and shingles), which does not tend to follow a marked seasonal pattern in the manner of influenza.¹¹ While the increased demands on GPs resulted in the withdrawal of some GPs from both surveillance programs (65 GPs participated in 2007, compared to 74 in 2006), the average GP response rate of 95% was considerable higher than previous years. For instance in 2005, average response rate was 85% and it was as low as 68% in 2006. As we have previously canvassed,⁷ high participation from a smaller number of participating practices may provide more representative surveillance data than larger numbers of practices with poorer response rates.

Acknowledgements

We gratefully acknowledge the participation of general practitioners and their practice staff in the sentinel surveillance program; their support is critical to its success.

As critical is the ongoing support and participation of the MMLS, and our particular thanks go to MMLS Directors, Ms Josie Adams and Ms Bronwyn Hawking.

We also thank others involved in the operation of the sentinel surveillance program, including the private pathology providers who facilitate transport of respiratory specimens from rural and regional general practices. Surveillance of laboratory-confirmed influenza is made possible through notifying laboratories (particularly the Viral Identification Laboratory at VIDRL) and medical practitioners throughout Victoria.

We also thank staff in the Communicable Disease Control Unit at the Department of Human Services for data entry and follow up of notifications data.

The Melbourne WHO Collaborating Centre for Reference and Research on Influenza is supported by the Australian Government Department of Health and Ageing.

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