The Influenza Surveillance Program in Western Australia, 2003

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Abstract

In the winter of 2003 Western Australia experienced its largest epidemic of influenza for at least five years, with activity peaking in August and September. The season was short resulting in very high numbers of cases during the peak weeks. Activity in country areas followed the peak of Metropolitan activity. Influenza A virus was detected in 28.3 per cent of the sentinel samples, and influenza B in less than one per cent. Both routine and sentinel detections and the overall estimates of influenza-like illnesses (ILI) seen by general practitioners at sentinel practices peaked in August and September 2003. The combination of influenza detections and an increase in ILI seemed to be the most accurate predictor of the beginning of winter influenza activity. There was a shift in age distribution for influenza A compared with 2003. Both the sentinel surveillance and routine samples demonstrated an increase of influenza in children and young adults. The majority of influenza A isolates were identified as A/Fujian/411/2002-like, a variant of the A/Moscow strain included in the vaccine. Despite this mismatch there did not seem to have been any noticeable increase in the risk of influenza infection in the vaccinated populations from the sentinel practices, nor was there a relative increase in disease among the highly vaccinated elderly population. A number of other respiratory viruses were identified as causes of influenza-like illness in the sentinel samples. Rhinoviruses and human metapneumovirus were the most common, the latter occurring mainly in adults. *Commun Dis Intell* 2004;28:169–174.

Keywords: Influenza, surveillance, Western Australia, Sentinel General Practice

Introduction

Influenza viruses are major respiratory pathogens, causing significant illness and mortality in Australia each winter. In 1999 a national influenza surveillance program was established in Australia. This included community-based surveillance, using sentinel general practices[1] and surveillance of routinely collected respiratory samples from paediatric and adult patients. This surveillance program provided both a system for detecting the entry and spread of new influenza strains and generated valuable information to medical and public health practitioners about influenza activity each winter.

The Division of Microbiology and Infectious Diseases at PathCentre in Western Australia is one of the Australian National Influenza Centres. A general practitioner based surveillance program has operated since 1999 with the support of the Health Department of Western Australia. In 2003 Western Australia experienced the worst outbreak of influenza for five years, almost exclusively due to an influenza A strain that was poorly matched to the vaccine strain. This report presents the results collected by the Western Australia Influenza Surveillance Program during the 2003 season, as well as routine influenza virus infections diagnosed at PathCentre.

Methods

Influenza surveillance was conducted in Western Australia for 25 weeks from the week beginning Monday 5 May (Week 19) to the week beginning 20 October (Week 43).

During the 2003 winter season, 16 medical practices were recruited to the Western Australia Influenza Surveillance Program. Figure 1 shows the locations of the sentinel practices within Western Australia. The majority (12) of these were based in the Perth metropolitan area. Country practices included Kalgoorlie (Goldfields), Busselton (Southwest), Tom Price (Pilbara) and Geraldton (Midwest). Participating general practitioners (GPs) recorded the number of patients seen with an influenza-like illness (ILI) each week. An ILI was defined as an acute upper respiratory tract infection characterised by fever (or feverishness), cough and fatigue.[2] Nose and throat swabs were collected from the first patient seen on

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Monday, Tuesday and Wednesday each week with an ILI of less than 96 hours duration. Swabs were placed in viral transport medium and were stored and transported at 4° C. For each sample the GP was asked to record the symptoms, date of onset of symptoms, vaccination history and to estimate the likelihood of the illness being due to infection with an influenza virus.

Specimens were tested at PathCentre using in-house polymerase chain reaction (PCR) assays which identified a number of common respiratory viruses including influenza A, B and C, parainfluenza types 1, 2 and 3, respiratory syncytial virus (RSV) and human metapneumovirus (hMPV). In addition to PCR testing, samples were inoculated onto two tissue culture cell lines [MDCK and human fibroblast (HF) cells] for virus culture. Rapid culture of samples for influenza was carried out by inoculating samples onto coverslips seeded with MDCK cells. Tubes were spun for 60 minutes at 4° C and then incubated at 37° C for two days. Cells were then fixed in PBS/acetone and any influenza virus isolates were identified by fluorescence using FITC-labelled specific monoclonal antibodies (DakoCytomation).

All influenza isolates were sent on dry ice to the WHO Collaborating Centre for Reference and Research on Influenza in Melbourne for full strain analysis.

Other virus isolates (including rhinoviruses, adenoviruses, enteroviruses) were identified initially by the type of cytopathic effect (CPE) they caused in HF cells and this result was confirmed by PCR.

Routine specimens

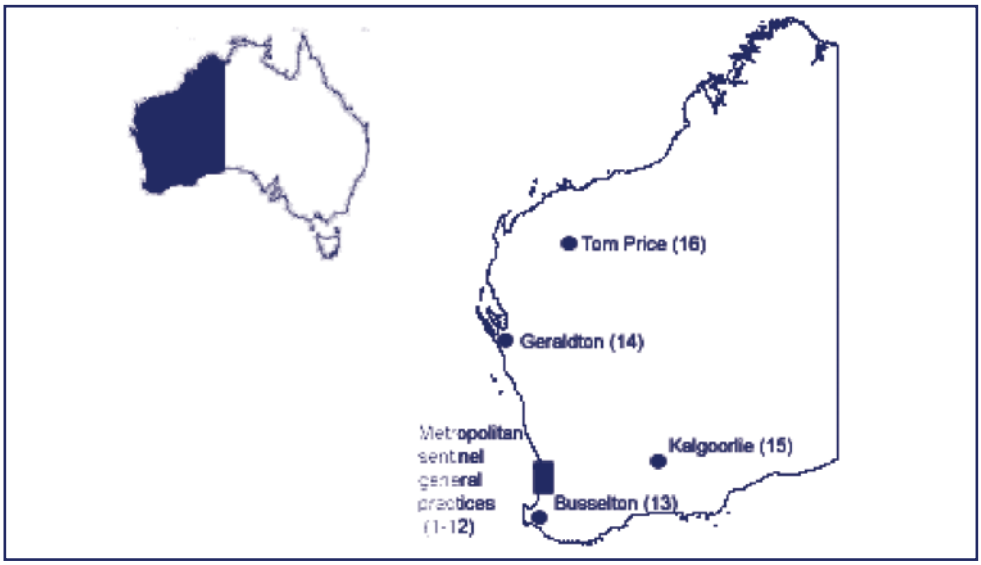
Routine samples are received at PathCentre throughout the year, from patients with respiratory infections from both metropolitan and country regions throughout Western Australia. If requested, these samples were tested for influenza and other respiratory viruses by the same methods as those used for the sentinel GP samples. We collated the total number of patients positive, either by PCR or virus culture, for influenza viruses and included these figures in the weekly reports. In addition, the number of blood samples sent for influenza serology was also recorded and reported weekly. Respiratory serology requests are usually undertaken for adults with proven or suspected lower respiratory tract infection.

Serologically diagnosed cases (influenza complement fixation tire of 1:160 or greater) were also recorded in order to improve the monitoring of influenza infections in adults.

Data collection and reporting

Results obtained from the general practitioner surveillance program as well as routine influenza detections from PathCentre and the Princess Margaret Hospital for Children were presented in the weekly Influenza News report that was sent out to the Health Department of Western Australia, all participating GPs and a number of other interested groups. As the number of practices reporting varied from week to week, the weekly information on ILIs was presented as the number of ILIs per reporting practices. Results of influenza detections (sentinel and routine) from PathCentre were also reported weekly to FluNet (available from: http://www.who.int/GlobalAtlas/home.asp).

Figure 1. Map of Western Australia showing the location of the 2003 sentinel general practices



Results

Sentinel general practices

A total of 276 samples were sent to PathCentre from 15 sentinel practices. One practice did not submit any samples this season. The ratio of males to females was approximately equal (135:141). Although 19 samples were sent with no date of onset recorded, over 97 per cent of the remaining samples were taken within the recommended 96 hours of onset of symptoms. According to the forms filled out by the doctors 203/276 (74%) of samples met the proposed case definition of fever, cough and fatigue. All patient samples were included in the analysis.

Influenza A virus was detected by PCR in 28.3 per cent of the sentinel samples. There was a single detection of influenza B virus. The positive rate was 36 per cent among patients who had request forms that showed symptoms meeting the case definition, but only 5.4 per cent for those who did not.

GPs were also asked to comment on their clinical impression of the patient and to estimate the likelihood of the patient's illness being caused by infection with an influenza virus (Table 1). The strength of the clinical impression of influenza showed a clear relationship to the actual influenza rates.

Influenza activity was substantially higher in 2003 than in the two previous years (Figure 2). Activity was even lower in 1999 and 2000 with reduced numbers of samples submitted by sentinel practices and only six and 15 influenza cases respectively, reported from sentinel samples. Influenza A activity in 2003 was first detected in early July and peaked in September and October (Weeks 35 to 39). Influenza B activity was detected only once. This was in the week beginning on 20 October 2003. The serology requests showed the first obvious rise but this preceded the beginning of the influenza season. Rises in ILI/practice and influenza detections from sentinel practices occurred 2–3 weeks later (Figure 3).

Figure 2. Comparison of influenza detections obtained from sentinel samples in 2001, 2002 and 2003

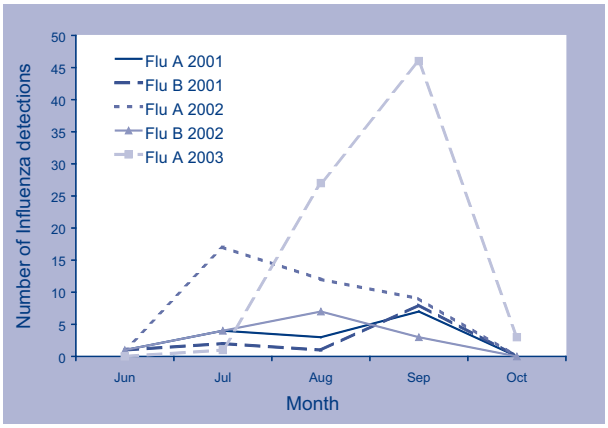


Figure 3. Incidence of sentinel GP influenza-like illnesses reporting and influenza detections, routine influenza detections and respiratory serology requests during the period of influenza surveillance, 2003

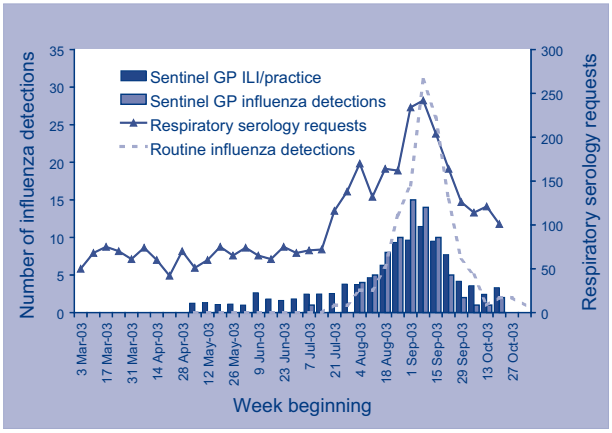
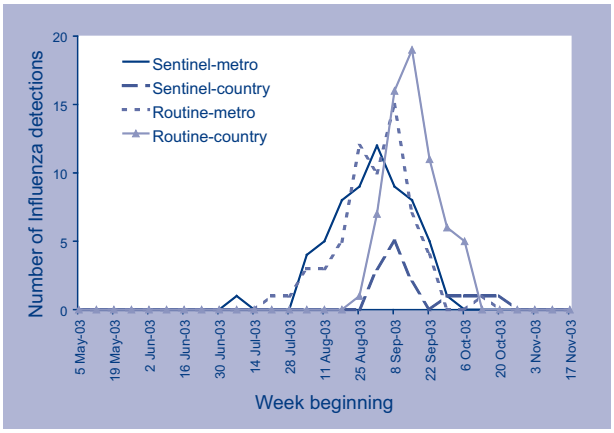


Table 1. Analysis of GP estimates of influenza virus infections in patients from sentinel practices

Respiratory virus detected	Almost certain influenza n=67		Probable influenza n=146		Likely influenza n=57		Not stated n=6	
	n	%	n	%	n	%	n	%
Influenza	38	56.7	35	24.0	6	10.5	0	0.0
Other virus	3	4.5	23	15.8	12	21.0	1	16.7
Not detected	26	38.8	88	60.3	39	68.4	5	83.3

When metropolitan and country areas were analysed separately (Figure 4) activity peaked in the Perth metropolitan area in September (week 35 to 37) and in late September and October in country areas (week 37 to 39).

Figure 4. Timing of detections of influenza A viruses from both routine and sentinel samples, 2003



Influenza A virus was detected in patients from all age groups but the largest percentage of positive samples were found in the 11–30 year age groups (43/89, 48%, Table 2).

Influenza infection was responsible for the illness in 32.3 per cent of the unvaccinated (68/211) compared with only 12.5 per cent (7/56) of the vaccinated individuals, i.e. unvaccinated patients with an ILI were 2.5 times more likely to have influenza than were vaccinated patients.

Routine samples received at PathCentre

Between 5 May 2003 and 26 October 2003 (the period of the surveillance program) there were 129 detections of influenza A and 2 detections of influenza B in the routine samples received by the PathCentre. These showed a time distribution similar to that shown by the sentinel general practices (Figure 4). Outside that period there was minimal influenza activity, with only five influenza A detections and two influenza B detections.

Typing of influenza isolates

In 2003 the laboratory referred a total of 111 influenza virus isolates to the WHO Collaborating Centre in Melbourne, of which 106 were type A, three type B and two could not be recovered. The latter were two influenza A isolates that were found by us to be positive for influenza virus, by PCR and fluorescence. Forty-five influenza isolates were obtained from the sentinel samples and 66 from routine specimens sent to the PathCentre. Forty-three of the sentinel positives were typed as influenza A, one as influenza B and one could not be recovered. Of the 66 isolations from routine samples, 63 were identified as influenza A, two as influenza B and one could not be recovered. The majority of influenza A isolates (104/106) isolated in Western Australia in 2003 were identified as the H3N2 subtype and were typed as A/Fujian/411/2002-like, a new variant of the A/Moscow strain that circulated in 2002. The remaining two isolates typed as A/Moscow/10/99-like. In 2003 relatively few cases of influenza B infection were detected in Western Australia and all were typed as B/Sichuan.

Table 2. Influenza detections in sentinel samples, 2003, by age group and vaccination status

Age group	Total samples	Influenza A				Influenza B			
		Positive samples	Male	Female	Vaccination history (Y/N/U)	Positive samples	Male	Female	Vaccination history (Y/N/U)
0–10	28	6	3	3	0/6/0				
11–20	46	26	17	9	2/23/1				
21–30	43	17	9	8	1/16/0				
31–40	53	10	4	6	1/7/2				
41–50	28	9	6	3	2/6/1				
51–60	32	9	5	4	0/9/0	1	1	0	0/1/0
>60	45	1	1	0	1/0/0				
Totals	275*	78	45	33	7/67/4	1	1	0	0/1/0

Vaccination history: N = not vaccinated, Y = vaccinated, U = unknown vaccination status of positive cases.

* Includes one patient of unknown age.

Other respiratory viruses

In addition to influenza A and B, 39 (14%) specimens of sentinel samples were positive for a number of other respiratory viruses: 5 parainfluenza, eight RSV, 11 human metapneumovirus, 17 rhinoviruses and one adenovirus. This included three dual infections, two with human metapneumovirus and influenza A, and one with parainfluenza 3 and influenza A.

Overview of the age distribution of influenza in 2003

The age distribution of the cases diagnosed as part of the sentinel general practitioner surveillance (Figure 5) showed a peak in adolescents and young adults that was not evident in 2002. Patients seen in the sentinel general practices are usually those with mild illness who seek attention from general practitioners and who may not necessarily have been sampled unless they were part of the surveillance. It does not necessarily reflect influenza distribution in more severely ill patients who warrant routine testing by their general practitioner or who present to hospital. Therefore the age distribution for influenza cases diagnosed from routine testing by culture, PCR or serology was also determined (Figure 6). This showed the expected peak in the elderly but, like the sentinel practice data, there was a relative increase in cases in the younger age groups compared with 2002.

The number of Influenza B cases was insufficient to comment on the age distribution.

Figure 5. Age distribution of patients with influenza confirmed by virus detection in surveillance samples from sentinel general practitioners

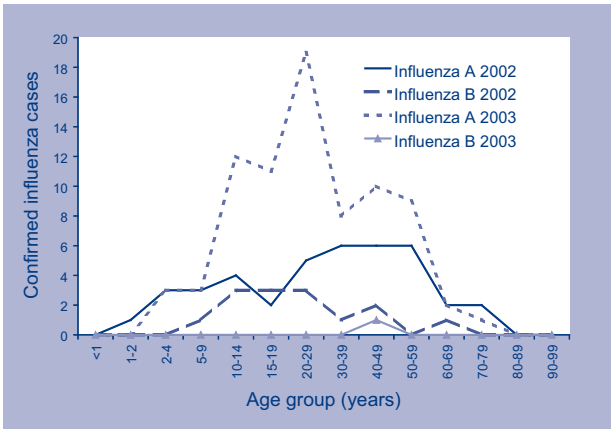
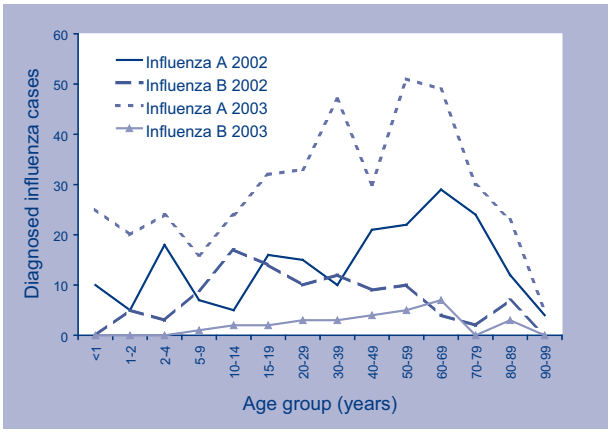


Figure 6. Age distribution of influenza cases diagnosed at PathCentre in 2002 and 2003, either by virus detection or serology



Discussion

In 2003 Western Australia experienced the largest influenza epidemic for at least five years. Additionally, the season was short resulting in very high numbers of cases during the peak weeks. The epidemic was predominantly caused by infection with influenza A H3 Fujian virus. Influenza A activity was first detected in the Perth metropolitan regions and then appeared to spread to country regions of the State. This increase in activity in country areas coincided with a decline in activity in Perth metropolitan areas.

The first indicator of the winter increase was a rise in the number of requests for respiratory serology, but this did not correlate with influenza activity in either sentinel or routine samples. However, there was significant RSV and rhinovirus activity detected in the routine PathCentre samples at that time (data not shown), which may have contributed to a rise in adult respiratory illness prior to the influenza season. The appearance of influenza in the sentinel samples accompanied by a rise in ILI seemed to give the earliest clear indication of the beginning of the influenza season. All indicators then rose together and peaked around the same time, including a secondary peak in the respiratory serology requests. The peak in routine influenza detections was slightly later than the peak in sentinel influenza activity. The higher proportion of country samples (which peaked later) among the routine positives compared with the sentinel positives would explain that difference (Figure 4).

The influenza A activity in 2003 showed an increase in disease in children and young adults compared with 2002, and this was seen in both the sentinel and routine samples. This may reflect an altered pathogenicity for this strain. Information from the following Northern Hemisphere winter indicated a possible increase in severe illness in children due to influenza A/H3 Fujian,[3] though this is not yet verified. Also our data is an underestimate of routinely diagnosed influenza in children, as it does not include children diagnosed at our major children's hospital. Therefore it is possible that the magnitude of the shift towards disease in children may also be underestimated.

The influenza A strain that emerged in 2003 (A/Fujian/411/2002-like) is an H3N2 drift variant of the A/Moscow/10/99-like strain that was circulating in 2002. The Australian vaccine for 2003 contained the A/Moscow strain and not the new variant and there was concern that vaccine-induced protection would be reduced for this strain. There was no obvious evidence of this in the GP sentinel data, where influenza was no more common as a cause of ILI in vaccinated individuals than it had been in previous years. Also a decline in vaccine effectiveness would be expected to result in a greater increase in illness among highly vaccinated population such as the elderly. The age distribution determined from the routine diagnostic samples did not show any relative increase in influenza among the highly vaccinated population aged 65 years or over and, in fact a lower proportion of cases occurred in those aged 60 years or older than in 2002 (Figure 6). However, we do not know whether the severity of illness was different. While this data is not conclusive, it does not indicate any substantial impact from the mismatch between the vaccine and the circulating strains.

In 2002 the dominant subtype of influenza B had been B/Hong Kong, which was included in the Australian vaccine for 2003. Relatively few cases of influenza B infection were detected in Western Australia and all were typed as B/Sichuan. In the absence of any significant activity it is not possible to speculate on the impact of the mismatch between the vaccine and the circulating strains.

A number of other respiratory viruses were also detected in sentinel samples. This was more likely to occur if the clinical impression reported by the GP was 'likely' or 'probable', rather than in the 'highly probable' group. It indicated that a strong clinical impression of influenza did largely separate influenza from other viruses. This may not necessarily apply to the same extent in seasons when influenza activity is lower or if the circulating strain causes milder illness. As in previous years, rhinoviruses were the most common respiratory pathogens besides influenza. It was interesting to see that hMPV was again detected in our surveillance population. The majority (8/11) occurred in patients aged 30 years or more, and activity occurred throughout the surveillance period. Relatively little is known about this virus as it was only identified in the past few years.[4] It is known to cause severe lower respiratory tract infections in young children, the elderly and immunosuppressed patients[5] and these data suggest that, like RSV, it circulates in the community as a mild respiratory illness of adults.

Acknowledgements

This surveillance program is funded by the Health Department of Western Australia.

We would like to thank all the participating general practitioners and their staff.

In addition, we thank all specimen reception staff and laboratory staff at PathCentre, Perth and country laboratories for arranging transportation and processing specimens. Thanks also to Robyn Wylie for her help preparing reports. We acknowledge the collaboration of the WHO Collaborating Centre for Reference and Research on Influenza.

References

1. Watts C, Kelly H. Fragmentation of influenza surveillance in Australia. *Commun Dis Intell* 2002;26:8–13. Erratum in: *Commun Dis Intell* 2002;26:288.

2. Thursky K, Cordova SP, Smith D, Kelly H. Working towards a simple case definition for influenza surveillance. *J Clin Virol* 2003;27:170–179.

3. Update: influenza-associated deaths reported among children aged <18 years—United States, 2003–04 influenza season. *MMWR Morb Mortal Weekly Rep* 2004;52:1286–1288.

4. van den Hoogen BG, de Jong JC, Groen J, Kuiken T, de Groot R, Fouchier RA, *et al.* A newly discovered human pneumovirus isolated from children with respiratory tract disease. *Nat Med* 2001;7:719–724.

5. Boivin G, Abed Y, Pelletier G, Ruel L, Moisan D, Cote S, *et al.* Virological features and clinical manifestations associated with human metapneumovirus: anew paramyxovirus responsible for acute respiratory tract infections in all age groups. *J Infect Dis* 2002;186:1330–1334.