Western Australian Influenza Surveillance Program

Annual Report, 2002

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The surveillance activities in this report are supported by funding from the Western Australian Department of Health

Background

Influenza viruses are major respiratory pathogens, causing significant illness and mortality in Australia each winter. Influenza viruses are RNA viruses that are members of the *Orthomyxoviridae* family (van Regermortel et al., 2000). Influenza A infects both humans and animals whereas influenza B only causes human disease. Unlike these two types, influenza C causes only mild human disease, usually in young children, and is not regarded as a major public health concern.

The surface of influenza viruses is covered with two types of proteins, known as the haemagglutinin (H) and the neuraminidase (N). These two proteins are continually mutating to produce new variants, a process referred to "antigenic drift" and this allows the virus to escape immunity induced by prior infection or vaccination. These new strains are responsible for causing the annual winter epidemics that vary in severity depending on the degree of antigenic change, inherent variability in the ability if that strain to cause disease, and whether environmental conditions are suited to spread of the virus. The world experiences two epidemic periods corresponding to the northern and southern hemisphere winters. However countries near the equator may experience either or both of these epidemics with a less clear seasonal pattern. The new strains that emerge each year are given the name of the city that first sends an isolate to one of the World Health Organization Collaborating Centres. In addition, influenza A virus can acquire genetic information from viruses carried by other species, particularly birds. In this way they can completely change their H subtype (and sometimes the N subtype), a process called "antigenic shift". It is these strains that cause worldwide pandemics of influenza as the population has no previous immunity to the new virus strain. Therefore influenza A strains are named according to the H and N subtype as well as the city that first isolated them. The subtypes of influenza A circulating in the population for the past 3 decades have been strains are known as A (H1N1) and A (H3N2).

In contrast to influenza A, influenza B viruses are more antigenically stable, though there are two distinct lineages of influenza B in the human population, known as the B/Victoria and B/Yamagata lineages. An important change occurred in 2002. In the 1990s the B/Victoria lineage disappeared from most regions (including Australia) but continued to circulate in Asia. Since then the southern hemisphere had only seen strains from the B/Yamagata lineage, most recently represented by B/Sichuan. However in late 2001the B/Victoria lineage re-emerged in the southern hemisphere (Asia) and in Australia the 2002 circulating strain was a member of this lineage named B/Hong Kong. This had not been predicted and the vaccine had contained the B/Sichuan strain, so that there were concerns that the relatively poor protection afforded by the vaccine would lead to a large outbreak of influenza B.

Surveillance Programs

In 1999 the Influenza Pandemic Planning Committee (IPPC) established by Communicable Diseases Network Australia New Zealand (CDNANZ) recommended the establishment of a national Influenza surveillance program. This was to include community-based surveillance, using sentinel general practices (Watts and Kelly, 2002) and surveillance of routinely collected respiratory samples from pediatric and adult patients. It was recognised that such surveillance would provide a system for detecting the entry and spread of new influenza strains. In addition it provides valuable information to medical and public health practitioners about influenza activity each winter. This helps guide decisions about vaccination, use of antiviral agents and likely impact on health resources. Influenza became a nationally notifiable disease in Australia in January 2001. The Division of Microbiology and

Infectious Diseases at PathCentre in Western Australia is one of the National Reference Laboratories for influenza in Australia. A general practitioner based surveillance program has operated since 2000 with the support of the Western Australian Department of Health.

During the 2002 Influenza season (April to October) there were up to 16 medical practices involved in the Influenza Surveillance program in WA. The majority (13) of the sentinel practices were based in the Perth Metropolitan area. Country practices included Kalgoorlie (Goldfields), Australind (Southwest) and Geraldton (Midwest). Samples were collected from patients and other respiratory pathogens. Information was also gathered on the number of influenza-like illnesses (ILIs) seen per week at each practice.

Participating General Practitioners (GPs) recorded the number of patients seen with an ILI each week. An ILI was defined as an acute upper respiratory tract infection characterised by fever (or feverishness), cough and fatigue. Nose and throat swabs were collected from the first patient seen each day (Mon-Thurs) with an ILI of less than 96 hours duration, up to a maximum of 3 samples per week. Swabs were placed in viral transport medium and were stored and transported at $4^{o}C$. For each sample the GP was asked to record the symptoms, date of onset of symptoms and vaccination history.

Samples were tested by PCR for 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). hMPV is a newly described respiratory virus, causing similar symptoms to RSV and appears to cause widespread infection in children. In addition to PCR testing, samples were inoculated onto tissue culture cell lines (both HF and monkey kidney tubes) for virus culture. Any virus isolates obtained were harvested and identified using a number of different techniques. Suspected influenza and parainfluenza virus isolates were initially separated by specific monoclonal antibodies. Influenza viruses were then subtyped as A(H1N1), A(H3N2), B/Hong Kong or B/Sichuan by carrying out a Haemagglutination Inhibition (HI) assay using antisera supplied by WHO. Isolates were then 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 and Herpes simplex viruses) were identified initially by the type of CPE they caused in human fibroblast (HF) cells and this identification was confirmed by PCR.

Additional information on activity of influenza and other respiratory viruses was obtained form the routine virus detections at PathCentre and data kindly provided by Princess Margaret Hospital for Children in Perth (PMH) via the Communicable Disease Section of the WA Department of Health.

Results and Discussion

Table 1 shows the number of samples sent by each sentinel practice and the number and types of viruses isolated during the 21-week program.

A total of 192 samples were sent to PathCentre from 14 sentinel practices. The ratio of males to females was approximately equal (101:91). It appeared that either the definition of ILI was not strictly applied and/or the reporting of symptoms on the request forms was incomplete. Although 97% of samples were taken within the recommended 96 hours of onset of symptoms only 126/192 (66%) met the proposed case definition of fever, cough and fatigue. All patients had at least one of the symptoms stated on the request forms (fever, cough, fatigue/malaise) and the majority of patients had 2-3 symptoms. Additional symptoms documented by the GPs included abdominal pain, dizziness, nausea, vomiting, aches/pains, headache, asthma and arthralgia.

Table 1. Number of specimens and virus detections from Sentinel Practices in 2002

Location	No	FLU A	FLU B	FLU C	PF1	PF2	PF3	RSV	HMPV	Rhino	Adeno	HSV	Total viruses
North Beach	51	4	1		2	1	1	4	6	4	1	1	25
Scarborough	44	3	5	1				2	2	5	3		21
Balcatta	22	1	4			1		2		1	3		12
Lesmurdie	17	9	2					2		3			16
Alexander Heights	15	3			1			3	2				9
Innaloo	11	6									2		8
Sorrento	9	3						1					4
Kalamunda	6	3						1		1			5
Ocean Reef	4	2											2
Spearwood	2	1			1								2
Mosman Park	1		1										1
Forrestfield	1	1											1
Bassendean	0												
Australind	8	2	2										4
Geraldton	1	1											1
Kalgoorlie	0												
Total	**192**	**39**	**15**	**1**	**4**	**2**	**1**	**15**	**10**	**14**	**9**	**1**	**111**

Key
No – number of specimens sent, FLU – influenza virus, PF – parainfluenza virus, RSV – respiratory syncytial virus,
hMPV – human metapneumovirus, HSV – Herpes simplex virus

Table 2 shows that the majority of patients who had influenza virus (145/192) had not been vaccinated. However, the majority of patients in this study (75%) had not been vaccinated against influenza virus (Table 3). Influenza infection was responsible for the illness in 32.9% of the unvaccinated compared with only 11.6% of the vaccinated individuals. Influenza A virus was detected in patients from all age groups whereas the majority of influenza B detections were in the 0-30 year age groups (Table 2).

Table 2. Influenza detections by age group and vaccination status in sentinel samples 2002

		FLU A				FLU B			
Age Group	**Number**	**Positives**	**M**	**F**	**Vacc (N/Y/U)**	**Positives**	**M**	**F**	**Vacc (N/Y/U)**
0-10	20	6	4	2	6/0/0	1	0	1	1/0/0
20-30	23	6	5	1	5/1/1	7	3	4	5/1/1
21-30	36	4	2	2	4/0/0	3	2	1	3/0/0
31-40	32	6	3	3	6/0/0	2	1	1	2/0/0
41-50	27	7	3	4	7/0/0	1	0	1	1/0/0
51-60	20	5	2	3	3/1/1	0	0	0	0
>60	34	5	3	2	3/2/0	1	1	0	1/0/0
TOTALS	**192**	**39**	**22**	**17**	**34/4/2**	**15**	**7**	**8**	**13/1/1**

KEY:
M = male, F = female, Vacc = vaccination history, N = not vaccinated, Y = vaccinated, U = unknown vaccination status

Table 3. Comparison of vaccination status to virus detections

Virus detection	**Vaccination status**		
	N	Y	U
Flu A,B C	48	5	3
Other Respiratory viruses	43	12	0
Negatives	55	26	1

N = not vaccinated, Y = vaccinated, U = unknown vaccination status

PCR – results from sentinel samples

Influenza viruses were the most commonly detected viruses obtained from the sentinel samples, influenza A being detected in 20% and influenza B in 8%. There was a single detection of influenza C virus. This virus has been detected regularly, though infrequently over many years. Subtyping of the influenza viruses is discussed below.

Figure 1 shows the timing of influenza detections (by specimen date) during 2002. Influenza A activity predominated in WA in 2002**.** Activity was detected from June to September with a peak in early July and consistent activity from July through to September. Overall lower levels of influenza B activity were detected from late June to late September 2002. Influenza C activity was detected only once in the week beginning 16/09/02. This year did not show a major epidemic of influenza, however activity was substantially higher than in 2001 (Figure 2). In addition, both Influenza A and B activity peaked earlier in 2002 and were more typical for our winter activity. Both 2000 and 2001 had shown low levels of unusually late influenza activity.

As can be seen from table 1 and figure 3, a variety of other viruses were detected. This was more likely if the person did not meet the definition of an ILI. RSV was the most frequently detected respiratory virus besides the influenza viruses. The majority (66%) of detections were obtained from patients over 40 years old illustrating the importance of milder respiratory illness in adults as a reservoir and mode of transmission of RSV in our community. The RSV activity coincided with influenza activity, which is the usual pattern. Not surprisingly rhinoviruses and adenoviruses were also quite common and occurred across the winter season. What was of great interest was the presence of hMPV in our surveillance population. Two were from children and eight from adults. Relatively little is known about this virus as it was only identified in the past few years (van den Hoogen *et al*, 2001). It is known to cause severe lower respiratory tract infections in young children, the elderly and immunosuppressed patients (Boiven *et al*, 2002) and this data suggests that, like RSV, it circulates in the community as a mild respiratory illness of adults. However, the hMPV activity was detected later in the season than the RSV activity.

Figure 1. Detection of influenza viruses in samples from sentinel general practices

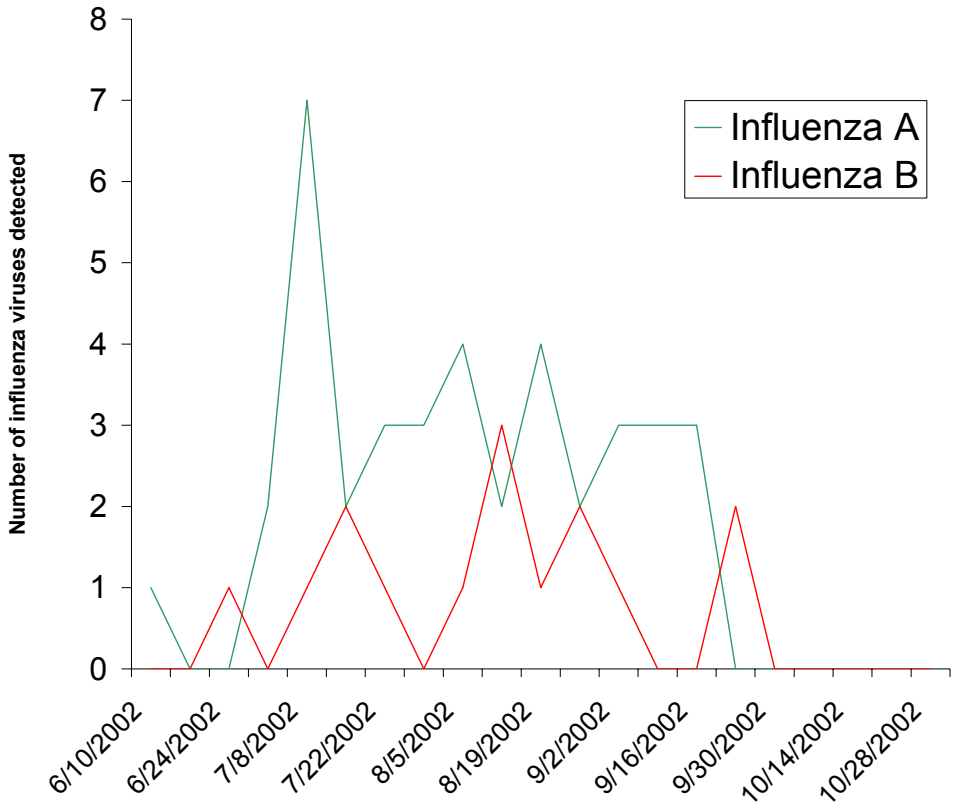


Figure 2. Comparison of Influenza isolations obtained from sentinel samples in 2001 and 2002

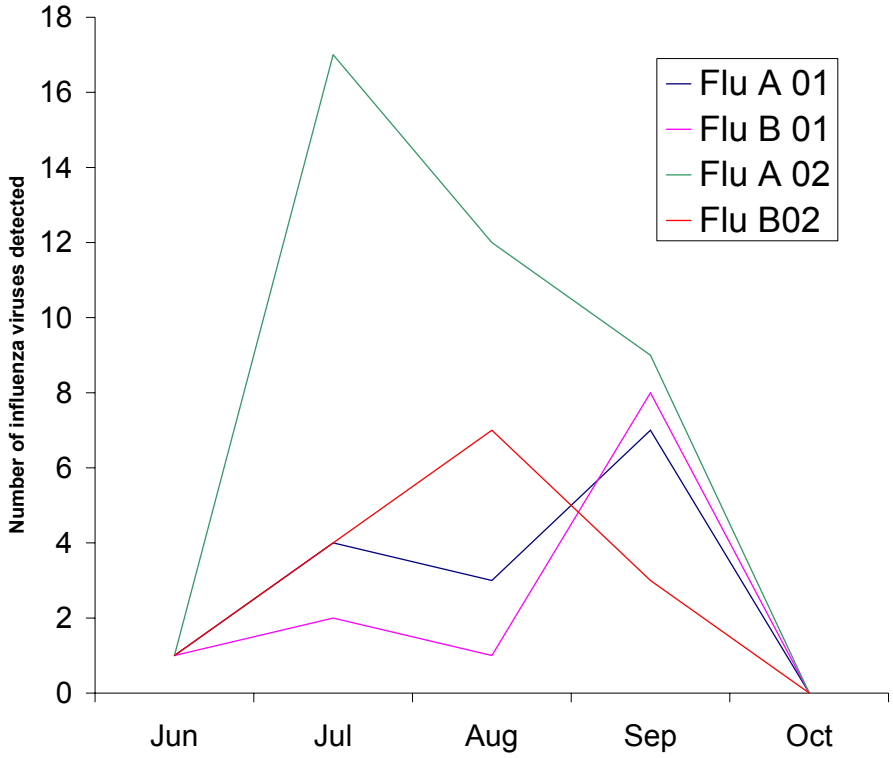
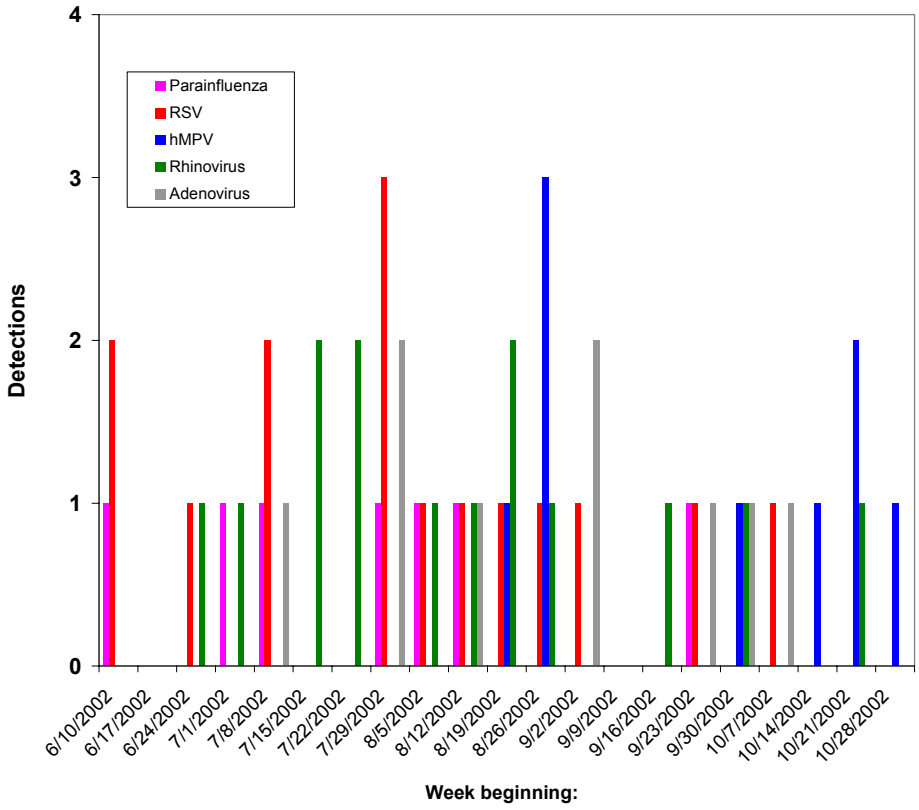


Figure 3. Detection of respiratory virus other than influenza from sentinel samples, 2002



Routine isolations of Influenza
From10/06/02 to 05/11/02 (the period of the surveillance program) there were 78 detections of influenza A and 26 detections of influenza B in the routine samples received by the PathCentre. These detections were made either by PCR or virus culture.

Virus Culture Results
In 2002 the laboratory obtained a total of 86 influenza virus isolates, 65 type A, 19 type B and three that could not be recovered by the WHO Collaborating Centre. The latter were three Influenza A isolates that were found by us to cause haemagglutination of guinea pig red blood cells in monkey kidney tubes and reacted against the influenza A monoclonal antibody. However, we also found them non-reactive in the HI assay. 27 isolates were obtained from the sentinel samples and 59 from routine specimens sent to the Perth PathCentre. Of the sentinel samples, 19 were identified as influenza A and 8 as influenza B

During 2002 all influenza A isolates were identified as A/Moscow/10/99-like, an H3N2 subtype of the virus. In the previous year low numbers of this subtype were obtained but the dominant strain in 2001 was an H1N1 subtype (A/New Caledonia/20/99-like). There were only 2 detections of this subtype in Australia in 2002 (Ref). In 2001 the dominant subtype of influenza B had been B/Sichuan but the first influenza B subtype obtained from Perth in 2002 was typed as B/Hong Kong. This was isolated from a specimen collected on the 13/03/02 and was the first isolate of this subtype obtained in Australia. Since then all influenza B isolates have been typed as B/Hong Kong. This subtype was only partially covered by the vaccine because the 2002 vaccine was based on the influenza A and B strains circulating in the region in 2001.

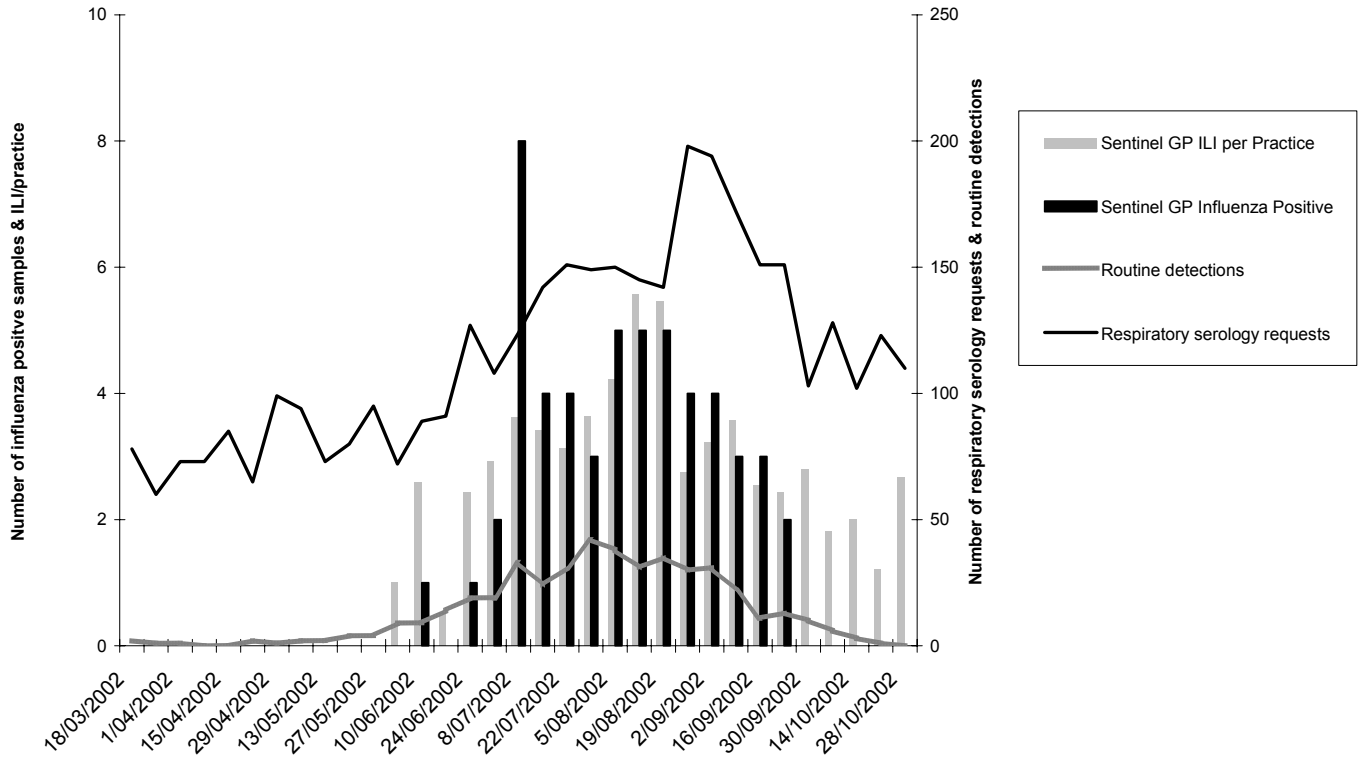
Influenza-like illnesses (ILIs)
The GPs were required to document the number of ILIs they saw each week (table 3). Results are expressed as ILIs per reporting practice, as the number of practices reporting varied from week to week. Figure 3 compares the amount of ILI/practice with numbers of sentinel and routine detections. The routine detections represent the total number of influenza detections at PathCentre (PCR and virus culture) and at PMH each week. Generally the trends were similar for all of these markers, though there was a single week with high numbers of influenza isolates without a large increase in ILI. This was due to a localised outbreak of influenza at a single sentinel site. The sentinel surveillance did accurately detect the beginning of the influenza season, and the combination of influenza detections and an increase in ILI seemed to be the most accurate predictor of the beginning of winter influenza activity. Both routine and sentinel detections were highest in July and August 2002 and the estimates of ILIs seen by GPs at sentinel practices peaked in August. Although the influenza detection rate fell in September and October patients continued to present with ILI, reflecting the ongoing circulation of other respiratory viruses such as hMPV, rhinoviruses, adenoviruses and RSV.

The number of requests for respiratory serology is included as these are usually undertaken for adults with proven or suspected lower respiratory tract infection. It showed that the number of requests rose significantly in the winter. There was a large rise early in September that we have not been able to adequately explain. The peak in serology requests occurred shortly after the peak of influenza activity. This may reflect the delay between when people are ill and when serum samples are collected. However, higher sampling rates often continue on beyond the end of the winter season perhaps due to heightened awareness and increased investigation rates or due to other circulating viruses.

Table 3. Weekly reporting of influenza-like illnesses from the influenza sentinel program, 2002

	Metropolitan				Country			
Week	Practices	ILI	ILI/ practice	Positive influenza	Practices	ILI	ILI/ practice	Positive influenza
01/07/02	4	19	4.75	1	1	1	1	1
08/07/02	11	44	4	8	2	3	1.5	0
15/07/02	11	41	3.73	4	1	0	0	0
22/07/02	13	44	3.38	4	1	0	0	0
29/07/02	9	37	4.11	3	2	3	1.5	0
05/08/02	12	55	4.58	4	1	0	0	1
12/08/02	12	71	5.92	3	2	7	3.5	2
19/08/02	11	61	5.55	5	2	10	5	0
26/08/02	10	32	3.20	3	2	1	0.5	1
02/09/02	12	42	3.5	4	1	0	0	0
09/09/02	11	43	3.91	3	1	0	0	0
16/09/02	12	33	2.75	3	1	0	0	0
23/09/02	13	34	2.62	2	1	0	0	0
30/09/02	9	28	3.11	0	1	0	0	0
07/10/02	11	20	1.82	0	1	0	0	0
14/10/02	10	22	2.20	0	1	0	0	0
21/10/02	13	17	1.31	0	1	0	0	0
28/10/02	5	16	3.20	0	1	0	0	0

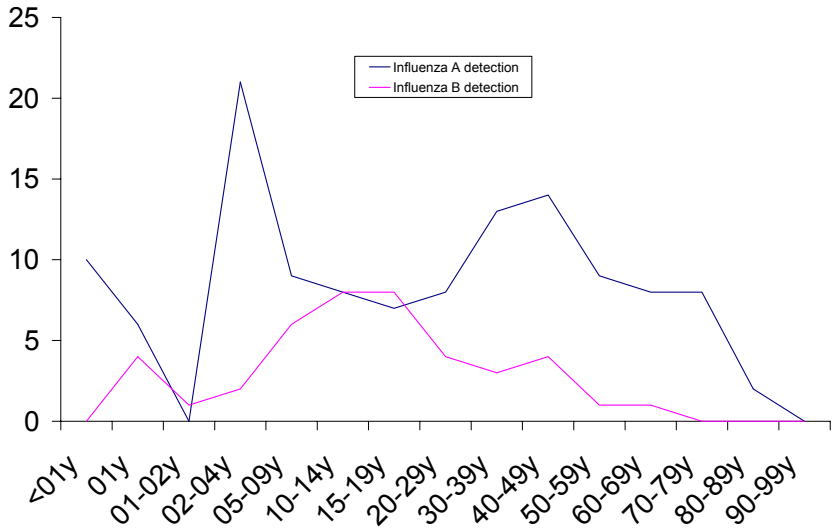
Figure 4. Incidence of Influenza detections and Influenza-like illnesses during the program



Overview of the Age Distribution of Influenza in 2002

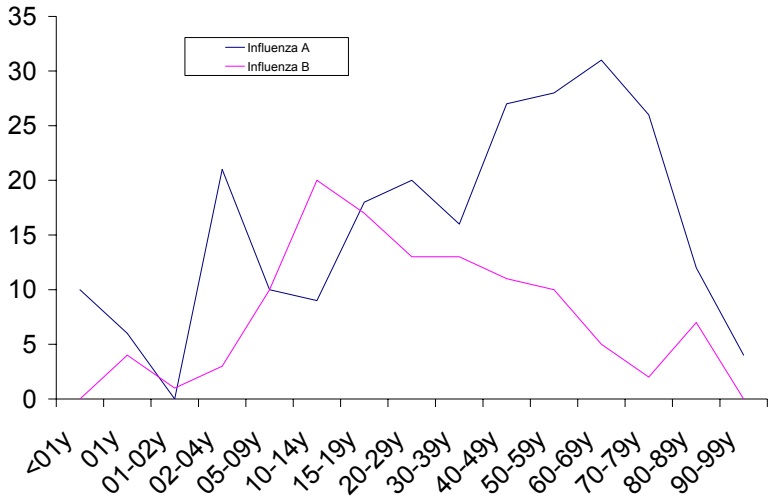
Total influenza detections at PathCentre were pooled to analyse the trends (figure 4). The relative number of paediatric detections is an underestimate, as this data does not include cases diagnosed at Princess Margaret Hospital for Children. It does demonstrate some interesting differences between the patterns of influenza A and influenza B infections. There were two peaks for influenza A detections, one in children under 10 years old, and the other in adults aged 30-49 years old, while influenza B peaked in the 10-19 year old groups.

Figure 5. Influenza virus detections in 2002 at PathCentre by age group



However, many cases of influenza are diagnosed serologically, especially in adults. Therefore it is important to include these cases to get an accurate picture of the distribution of disease in the adult community. Nearly all were diagnosed based on a single high complement fixation titre (1:160 or higher) and a few based on rising titres. When these are added to the influenza detection data (figure 5) it clearly illustrates the differences between influenza A and influenza B, with the former showing a peak in the 50-79 year olds, while influenza B had a much broader peak in younger adults.

Figure 6. Total influenza infections diagnosed in 2002 at PathCentre by age group



Conclusions

- Moderate levels of influenza activity were seen in WA in 2002, with activity peaking in July and August.
- Influenza A virus was detected in 20% of the sentinel samples, and influenza B in 8%. There was a single influenza C detected.
- All influenza A isolates were identified as A/Moscow/10/99-like, an H3N2 subtype of the virus. The dominant H1N1 strain that circulated in 2001 was not present this year.
- All influenza B isolates have been typed as B/Hong Kong/330/2001. This is different to 2001 when the dominant strain was B/Sichuan/379/99-like. However, despite the mismatch between the vaccine strain (B/Sichuan) and the circulating strain there was no major epidemic of influenza B. This may be due to partial protection from the vaccine or simple fortuitous.
- In this population, influenza was three times more likely to be the cause of respiratory illness among the unvaccinated patients compared with the vaccinated ones.
- In the adolescent and adult population, influenza A peaked in those over 40 years old, while influenza B peaked in younger adults and adolescents.
- Other respiratory virus detected were RSV, rhinoviruses, human metapneumovirus, parainfluenzaviruses (1.2 and 3), adenoviruses and enteroviruses.

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WHO Collaborating Centre for Reference and Research on Influenza, www.influenzacentre.org.au.