Influenza A testing and detection in patients admitted through emergency departments in Sydney during winter 2009: implications for rational testing

Andrew Jardine, Stephen J Conaty, Michelle A Cretikos, Wei-Yuen Su, Iain B Gosbell and Sebastiaan J van Hal

ABSTRACT

Aim: To examine factors associated with testing and detection of influenza A in patients admitted to hospital for acute care during the winter 2009 pandemic influenza outbreak.

Design, setting and participants: Retrospective observational study of patients who were tested for influenza A after being admitted to hospital through emergency departments of the Sydney South West Area Health Service from 15 June to 30 August 2009.

Main outcome measures: The association of factors such as age, diagnosis at admission, hospital and week of admission with rates of testing and detection of influenza A.

Results: 17 681 patients were admitted through nine emergency departments; 1344 (7.6%) were tested for influenza A, of whom 356 (26.5%) tested positive for pandemic influenza. Testing rates were highest in 0–4-year-old children, in the peak period of the outbreak, and in patients presenting with a febrile or respiratory illness. Positive influenza test results were common across a range of diagnoses, but occurred most frequently in children aged 10–14 years (64.3%) and in patients with a diagnosis at admission of influenza-like illness (59.1%). Using multivariate logistic regression, patients with a diagnosis at admission of fever or a respiratory illness at admission were most likely to be tested (odds ratios [ORs], 15 [95% CI, 11–21] and 17 [95% CI, 15–19], respectively). These diagnoses were stronger predictors of influenza testing than the peak testing week (Week 4; OR, 7.0 [95% CI, 3.8–13]) or any age group. However, diagnosis at admission and age were significant but weak predictors of a positive test result, and the strongest predictor of a positive test result was the peak epidemic week (Week 3; OR, 120 [95% CI, 27–490]).

Conclusion: The strongest predictor of a clinician's decision to test for influenza was the diagnosis at admission, but the strongest predictor of a positive test was the week of admission. A rational approach to influenza testing for patients who are admitted to hospital for acute care could include active tracking of influenza testing and detection rates, testing patients with a strong indication for antiviral treatment, and admitting only those who test negative to "clean" wards during the peak of an outbreak.

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During the 2009 southern hemisphere winter, testing for influenza initially overwhelmed reference laboratory resources.[1] Most of this initial testing was for non-hospitalised patients, but, as the pandemic (H1N1) 2009 influenza outbreak progressed, the demand for influenza testing (as well as testing for respiratory viruses in general) in non-reference public laboratories for patients admitted to hospital increased dramatically.[2]

The first locally acquired Australian case of pandemic influenza was confirmed on 22 May 2009.[3] By 17 June 2009, there was sustained community transmission and the purpose of testing for influenza changed from public health containment to early detection and treatment of those at risk of severe influenza-related illness, particularly those hospitalised with an influenza-like illness.[4] Influenza activity peaked in New South Wales in early July.[2]

Prospective studies identifying clinical factors that predict influenza infection have mainly been conducted in ambulatory care settings and have shown that — although it is difficult to confirm or exclude influenza on clinical grounds — fever, cough and acute onset are, at least in adults, useful clinical features.[5] The hospital and mortality burden of influenza is well recognised,[6] but studies aimed at identifying clinical features that predict influenza infection in hospital settings, which could guide rational testing and empiric treatment, are scarce. The epidemic situation in NSW during winter 2009 provided a natural opportunity to study questions related to influenza testing in patients admitted to hospital, including which factors influence clinicians' decisions to test for influenza and whether detection of influenza could be better predicted.

We examined whether the likelihood of testing for and detection of influenza A in patients admitted to hospital for acute care was associated with factors such as age, diagnosis at admission, hospital and week of admission, and looked for factors that could be used to provide rational guidance for influenza testing.

METHODS

The Sydney South West Area Health Service (SSWAHS) covers central and south-western Sydney, and incorporates nine public hospitals with emergency departments (EDs) that serve a total population of 1.4 million people. Patients admitted to hospital through any ED in the SSWAHS between 15 June and 30 August 2009 were enrolled in the study. Data were provided by NSW Health using the NSW Emergency Department Data Collection.

Two public hospital laboratories within the Sydney South West Pathology Service — at Liverpool Hospital and Royal Prince Alfred Hospital — performed all the influenza testing. Diagnostic testing for influenza A and pandemic influenza subtyping were similar in both laboratories. Following total nucleic acid extraction from nasopharyngeal swabs, influenza A and pandemic influenza were confirmed by polymerase chain reaction using assays which target the matrix protein (influenza A) and nucleocapsid protein gene segment (pandemic influenza) (Influenza 4, Influenza 6 and Respiratory pathogens 12 Easy-Plex assay kits [AusDiagnostics, Sydney, NSW]).[7]

ED admissions were linked to laboratory data using each patient's medical record number, sex and age. For patients with more than one ED admission, the admission corresponding with influenza testing was selected for linkage; for those who were not

tested, the first admission was selected. All patients for whom an influenza test had been requested but not performed were recorded as not tested. Patients who died in the ED from any cause were excluded.

The Systematized Nomenclature of Medicine – Clinical Terms (SNOMED CT) admission diagnosis code for each patient was categorised to one of 13 diagnosis categories (Box 1).[8] These included four main categories (respiratory conditions, fever, cardiac conditions and other conditions). Respiratory conditions were further divided into 10 diagnosis subcategories.

Rates of testing for influenza A and rates of detection of influenza A (per 100 patients admitted through EDs) were analysed by week of admission, hospital, age group, sex, admission destination (general ward or critical care unit), weekday of presentation, time of day of presentation, triage category, laboratory location (onsite or offsite) and admission diagnosis category. Statistical significance was assessed using the χ^2 test.

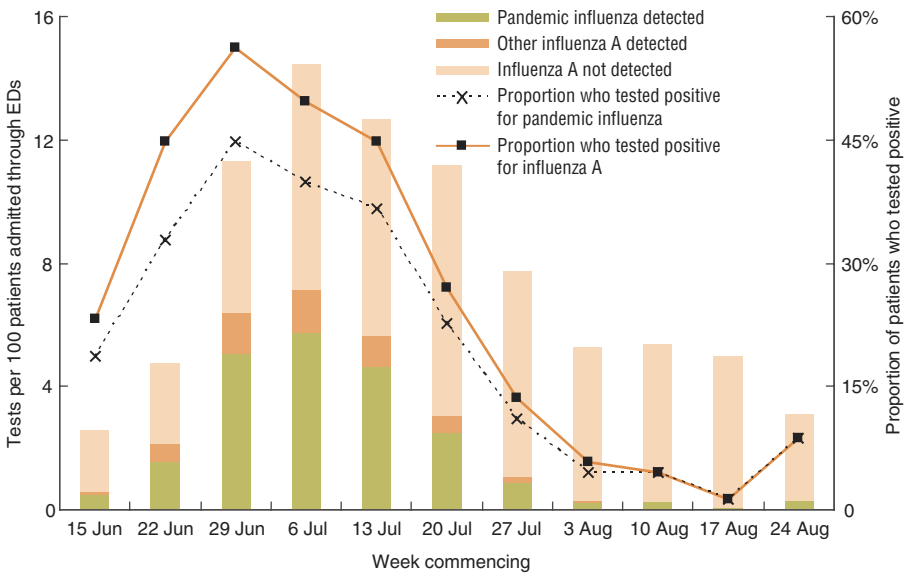
Multivariate logistic regression using STATA version 10 SE (StataCorp, College Station, Tex, USA) was performed to test whether the study factors were associated with testing for influenza A and, in patients who were tested, detection of influenza A. Variables that were significant in the univariate analysis were included in the multivariate logistic regression analyses. Non-significant associations ($P > 0.05$) between these factors and the outcome were dropped until the simplest model of the association between significant study factors and these two outcomes was obtained. For both testing and detection of influenza A, the final model included only age group, week of admission and diagnosis category. Regression analyses were also adjusted for clustering by admitting hospital.

The study was approved by the SSWAHS Ethics Review Committee (RPAH Zone), and no formal funding was obtained to conduct the study.

1 Admission diagnosis categories and examples of Systematized Nomenclature of Medicine – Clinical Terms (SNOMED CT) diagnosis codes for each category

Diagnosis category	Examples of SNOMED CT admission diagnosis codes
Respiratory condition	
Asthma	Asthma, acute asthma, exacerbation of asthma
Bronchiolitis	Bronchiolitis
Chronic lung disease	Chronic obstructive pulmonary disease, chronic obstructive airways disease, chronic airflow limitation, emphysema
Influenza-like illness	Influenza, influenza-like illness
Lower respiratory tract infection	Lower respiratory tract infection, chest infection, recurrent chest infection, bronchitis
Pneumonia	Pneumonia, aspiration pneumonia, lobar pneumonia, community-acquired pneumonia
Shortness of breath	Shortness of breath, breathing difficulty, respiratory failure, breathlessness
Upper respiratory tract infection	Upper respiratory tract infection, cough, tonsillitis, otitis media
Viral illness	Viral illness, viral infection, viral disease
Other respiratory condition	Pleural effusion, haemoptysis, pneumothorax, lung cancer, pulmonary embolism
Fever	Fever, febrile convulsions, pyrexia, febrile neutropenia
Cardiac condition	Myocardial infarction, congestive cardiac failure, acute pulmonary oedema, rapid atrial fibrillation, supraventricular tachycardia.
Other condition	All other admission diagnosis codes such as acopia, fall, fracture, injury, mental illness, confusion, stroke, headache, back pain, dehydration, and urinary tract infection.

2 Rates of testing for and detection of influenza A in patients admitted through EDs in the SSWAHS, and proportions of patients who tested positive, by influenza A subtype and week of specimen collection, 15 June to 30 August 2009

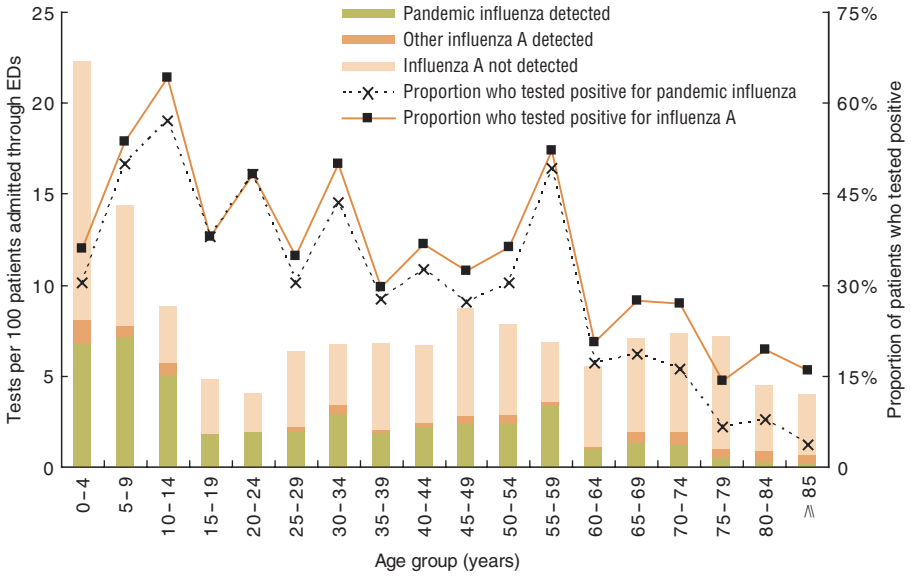


ED = emergency department. SSWAHS = Sydney South West Area Health Service. ◆

RESULTS

Between 15 June and 30 August 2009 inclusive, 17 787 unique patients were admitted to hospital through EDs in the SSWAHS. Of these patients, 106 died in the ED and were excluded. Of the remaining 17 681 patients, 1387 (7.8%) had an influenza test requested, but 43 of the requested tests were not performed. Of the 1344 patients who were tested for influenza (7.6% of the unique patients), 441 (32.8%) tested positive for influenza A and 356 (26.5%) tested positive for pandemic influenza. For those tested, the median time from admission to sample collection was 1 day. On univariate analysis, rates of testing and detection of influenza A were significantly associated

3 Rates of testing for and detection of influenza A in patients admitted through EDs in the SSWAHS, and proportions of patients who tested positive, by influenza A subtype and age group, 15 June to 30 August 2009



ED = emergency department. SSWAHS = Sydney South West Area Health Service. ◆

4 Patients admitted through emergency departments in the Sydney South West Area Health Service who were tested for influenza A and who tested positive for influenza A , by diagnosis at admission, 15 June to 30 August 2009

	Patients		
Diagnosis category	No.	No. (%) who were tested for influenza A	No. (%) who tested positive for influenza A
Respiratory conditions	3247	888 (27.3%)	302 (34.0%)
Asthma	371	80 (21.6%)	28 (35.0%)
Bronchiolitis	168	63 (37.5%)	11 (17.5%)
Chronic lung disease	361	100 (27.7%)	29 (29.0%)
Influenza-like illness	93	66 (71.0%)	39 (59.1%)
Lower respiratory tract infection	266	80 (30.1%)	30 (37.5%)
Pneumonia	684	228 (33.3%)	71 (31.1%)
Shortness of breath	639	139 (21.8%)	42 (30.2%)
Upper respiratory tract infection	293	78 (26.6%)	32 (41.0%)
Viral illness	122	36 (29.5%)	18 (50.0%)
Other respiratory conditions	250	18 (7.2%)	2 (11.1%)
Fever	434	122 (28.1%)	59 (48.4%)
Cardiac conditions	2261	71 (3.1%)	9 (12.7%)
Other conditions	11739	263 (2.2%)	71 (27.0%)
Total	17681	1344 (7.6%)	441 (32.8%)

with age, week of admission, diagnosis category, and triage category ($P < 0.02$ for all, χ^2 test).

Testing rates varied with time, and the highest testing rate occurred in the period 6 July to 12 July (Week 4), when 254 of 1639 patients (15.5%) were tested (Box 2). The influenza A detection rate peaked in the period 29 June to 5 July (Week 3), when influenza A was detected in 113 of 201 patients (56.2%) who were tested (Box 2).

Rates of testing for influenza A and rates of detection of both influenza A and pandemic influenza varied by age group (Box 3). Although the proportion of patients tested was highest in the 0–4-years age group (299 of 1342; 22.3%), the rate of influenza A detection was highest in children aged 10–14 years (18 of 28; 64.3%). Older patients (≥ 60 years) were less likely to be infected with pandemic influenza than younger patients (Box 3).

Similarly, rates of testing and detection of influenza A varied by illness severity. Patients assigned to triage category 2 were more likely to have a test performed than patients assigned to triage category 5 (10.2% [355/3483] v 2.5% [8/326]; $P < 0.001$, χ^2 test). In contrast, patients assigned to lower triage categories were significantly more likely to test positive for influenza A compared with patients assigned to higher triage categories ($P = 0.02$, χ^2 test).

The proportion of patients who were tested for influenza A varied by diagnosis category (Box 4), with testing rates highest for patients with fever (28.1% tested) or a respiratory condition (27.3% tested). Among these patients, influenza A was most commonly detected in those diagnosed with influenza-like illness (59.1%), viral illness (50.0%) or a fever (48.4%). Within the other respiratory categories, 31.1% of those diagnosed with pneumonia and 30.2% with shortness of breath tested positive, while influenza A was relatively uncommon among patients with bronchiolitis (17.5%) (Box 4).

Multivariate regression analysis (Box 5) showed that diagnosis category had the strongest association with testing for influenza A. For patients with a febrile or a respiratory condition, the odds of being tested were 15 to 17 times higher compared with patients who did not have a febrile, respiratory or cardiac condition at admission. Controlling for age and diagnosis category, the odds of a patient being tested in the period 6 July to 12 July (Week 4) were sevenfold higher than for 15 June to 21 June (Week 1). Week of admission had by far the strongest association with detection of influenza A. The odds of a positive influenza A result were 120 times higher in the period 29 June to 5 July (Week 3) compared with the period 17 August to 23 August (Week 10).

DISCUSSION

We examined the factors associated with testing for and detection of influenza A in patients admitted to hospital through EDs in

the SSWAHS during the winter 2009 pandemic influenza outbreak. Overall, 7.6% of admitted patients were tested, of whom 32.8% tested positive for influenza A. Testing peaked at 15.5% in Week 4 (6 July to 12 July), while the proportion of patients who tested positive for influenza A peaked at 56.2% in Week 3 (29 June to 5 July).

In a case series of patients admitted to hospital with confirmed influenza A during the 2009 southern hemisphere winter, classic features such as cough and fever were commonly reported, but the spectrum of illness was broad.[9] Risk factors for severe disease, including pregnancy, airways disease, diabetes and high body mass, have been reported in an intensive care unit case series[10] and an epidemiological summary of the first winter wave of the pandemic influenza outbreak.[2] Our observational study design, in which two routine datasets were matched for a large sample of patients, enabled us to make broad conclusions about the approach of clinicians to testing for influenza and the features predictive of a positive test result. It only included patients who were admitted to hospital through EDs, hence the results may not be applicable to outpatients and to patients in non-acute-care settings such as general practice. In addition, clinical information, in the form of the SNOMED CT diagnosis codes, was provided at triage. Many of these codes only provide syndromic descriptions of the reason for admission, and the diagnosis codes entered by ED staff at the time of patient admission may not always accurately capture the final diagnosis.[11] Nevertheless, the decision to test for influenza is usually made shortly after presentation; therefore, the diagnosis at admission is arguably a more accurate representation of the information available to the clinicians when they decide whether to test for influenza.

5 Association between age group, week of admission and diagnosis category and rates of testing for and detection of influenza A in patients admitted through EDs in the Sydney South West Area Health Service, 15 June to 30 August 2009

	Adjusted odds ratio (95% CI)*	
	Tested for influenza A	Influenza A detected
Age group (years)		
0–4	2.6 (0.9–7.4)	3.7 (2.0–6.8)
5–14	2.7 (1.0–7.2)	6.0 (2.4–14)
15–24	1.6 (0.8–3.3)	2.9 (1.6–5.4)
25–39	2.5 (1.7–3.7)	2.9 (2.0–4.0)
40–59	2.5 (1.9–3.4)	3.3 (2.3–4.6)
60–79	1.8 (1.5–2.2)	1.4 (1.0–1.8)
⩾ 80	1.0†	1.0†
Week of admission		
Week 1 (15 Jun – 21 Jun)	1.0†	20 (5.6–74)
Week 2 (22 Jun – 28 Jun)	2.0 (1.2–3.4)	61 (6.7–560)
Week 3 (29 Jun – 5 Jul)	5.1 (3.0–8.6)	120 (27–490)
Week 4 (6 Jul – 12 Jul)	7.0 (3.8–13)	98 (22–430)
Week 5 (13 Jul – 19 Jul)	6.3 (4.0–9.9)	76 (13–450)
Week 6 (20 Jul – 26 Jul)	6.5 (4.2–9.9)	37 (7.0–200)
Week 7 (27 Jul – 2 Aug)	4.7 (2.8–7.8)	15 (1.8–130)
Week 8 (3 Aug – 9 Aug)	3.0 (1.8–5.1)	5.9 (0.6–63)
Week 9 (10 Aug – 16 Aug)	2.9 (1.5–5.5)	3.8 (0.3–55)
Week 10 (17 Aug – 23 Aug)	2.4 (1.4–4.3)	1.0†
Week 11 (24 Aug – 30 Aug)	1.6 (1.1–2.2)	8.5 (0.4–170)
Diagnosis category		
Respiratory condition	17 (15–19)	3.1 (1.2–7.5)
Asthma	11 (8.9–13)	3.1 (1.5–6.4)
Bronchiolitis	24 (15–38)	1.3 (0.3–4.7)
Chronic lung disease	19 (14–26)	3.1 (1.0–9.2)
Influenza-like illness	81 (48–140)	7.1 (2.5–20)
Lower respiratory tract infection	22 (18–27)	4.1 (1.6–10)
Pneumonia	23 (19–27)	2.4 (1.0–6.0)
Shortness of breath	13 (9.8–17)	2.6 (1.1–6.1)
Upper respiratory tract infection	15 (10–22)	3.3 (1.1–9.9)
Viral illness	15 (9.9–22)	4.5 (2.7–7.5)
Other respiratory condition	3.5 (2.1–5.9)	0.8 (0.2–2.7)
Fever	15 (11–21)	3.6 (1.5–8.9)
Cardiac condition	1.5 (1.0–2.2)	1.0†
Other condition	1.0†	1.7 (0.8–3.8)

* Adjusted for clustering by admitting hospital. † Reference category. ◆

So, what factors guided clinicians in deciding whether to test for influenza in patients admitted to hospital for acute care? Controlling for age, week of admission, and illness severity, clinical presentations with a febrile or respiratory illness (especially patients presenting with an influenza-like illness) were the strongest predictors for influenza testing. The two other factors guiding testing were age and week of admission. The association with age was surprisingly weak; older patients (⩾ 80 years) were least likely to be tested, with minor differences in testing rates among the other age groups. Week of admission had a moderate influence; and testing lagged behind the highest odds for a positive test by 1 week, suggesting that clinicians are influenced by recent positive test results.

So, what factors were most predictive of a positive influenza test result? Week of admission had the strongest association with influenza A detection, outweighing age and diagnosis category. The strong seasonality of influenza is well described,[12,13] but the strength of this association is surprising. Although testing intensity was highest in children under 10 years of age, the highest rates of influenza detection were in 10–14-year-old children. This concurs with epidemiological data suggesting a higher incidence of pandemic influenza infection in school-aged children.[2,14-16] Similarly, the lower rates of testing and detection in older patients, especially those 80 years and older, suggests a low incidence of disease in older patients, possibly due to pre-existing immunity.[2,14,17-21]

After controlling for age and week of admission, the association between diagnosis at admission and a positive test result was weak. A diagnosis of fever or a respiratory condition (excluding the category "other respiratory condition") increased the odds of a positive test result. However, only an influenza-like illness diagnosis stood out in both univariate and logistic regression analyses, with a 59.1% rate of influenza A detection and sevenfold higher odds of a positive influenza test result compared with cardiac conditions. Rates of testing of patients with non-respiratory and non-febrile conditions were low (2.2%–3.1%), but detection rates for these patients were comparable to respiratory diagnosis categories. This result

highlights the varying presentations of influenza. In addition, it confirms the insensitivity of any particular influenza case definition, because the broadest definition (anyone with fever or a respiratory condition) identified 81.9% (361/441) of influenza cases in our study. Thus, to prevent hospital transmission, especially in patients at risk of severe influenza-related illness (such as those in haematology and oncology wards), strict infection-control procedures are required for all patients.[22,23]

Testing individuals who present to EDs during an influenza outbreak is only useful if a positive result will guide the use or discontinuation of an intervention. For maximum utility, a rapid test turnaround time is essential. Testing should be selective, as testing all potential cases in peak periods (about 3681 patients were admitted with a febrile or respiratory condition during our study period) could overwhelm the capacity of laboratories to perform tests in a timely manner.

So, what should be the rational approach to influenza testing for patients who are admitted to hospital for acute care? First, we suggest that there could be a role for intermittent laboratory testing to complement existing sources of surveillance information.[24] Documenting the upswing, peak and tail of the outbreak with active tracking of testing and detection rates could be a cost-effective method to guide clinical management of influenza, particularly the use of anti-influenza therapy.

Second, during an influenza outbreak it is prudent to test patients with a strong indication for antiviral treatment, such as immunocompromised patients and those who require intensive care. Anti-influenza treatment should be initiated in all these patients, with cessation of antiviral therapy possible following a negative influenza test result.

Finally, we suggest that the main role of testing is to provide guidance for cohorting hospitalised patients during an influenza outbreak, and thereby prevent hospital transmission. Testing should be used to ensure that certain wards, designated as "clean", remain free of influenza by restricting patient movement into these wards to only those who test negative to influenza or have received 72 hours of antiviral therapy.

In our study, the strongest predictor of a clinician's decision to test for influenza was the diagnosis at admission, but the strongest predictor of a positive test was the week of admission. Hence, diagnosis at admission provides poor guidance for rational testing. A testing strategy that includes testing on the basis of outbreak progression should be considered.

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COMPETING INTERESTS

None identified.

AUTHOR DETAILS

Andrew Jardine, PhD, MAE, Epidemiologist[1]
Stephen J Conaty, MB BS, MPH, FAFPHM, Acting Director[1]
Michelle A Cretikos, MPH, PhD, FAFPHM, Medical Epidemiologist[1,2]
Wei-Yuen Su, MB BS, Microbiology Registrar[3]
Iain B Gosbell, MD, FRACP, FRCPA, Foundation Professor of Microbiology and Infectious Diseases,[4] and Clinical Academic[5]
Sebastiaan J van Hal, MB ChB, FRACP, FRCPA, Microbiology and Infectious Diseases Specialist[5]

1 Public Health Unit, Sydney South West Area Health Service, Sydney, NSW.
2 School of Public Health, University of Sydney, Sydney, NSW.
3 Department of Microbiology, Sydney South West Pathology Service — Royal Prince Alfred Hospital, Sydney, NSW.
4 Microbiology and Infectious Diseases Unit, School of Medicine, University of Western Sydney, Sydney, NSW.
5 Department of Microbiology and Infectious Diseases, Sydney South West Pathology Service — Liverpool Hospital, Sydney, NSW.

Correspondence:
stephen.conaty@email.cs.nsw.gov.au

REFERENCES

1 Grayson ML, Johnson PD. Australia's influenza containment plan and the swine flu epidemic in Victoria. *Med J Aust* 2009; 191: 150.
2 New South Wales public health network. Progression and impact of the first winter wave of the 2009 pandemic H1N1 influenza in New South Wales, Australia. *Euro Surveill* 2009; 14 (42): pii = 19365.
3 Australian Government Department of Health and Ageing. Alert level raised to 'CONTAIN' [media release]. 22 May 2009. http://www.healthemergency.gov.au/internet/healthemergency/publishing.nsf/Content/news-022 (accessed Sep 2009).
4 Australian Government Department of Health and Ageing. New pandemic phase 'PROTECT' [media release]. 17 Jun 2009. http://www.healthemergency.gov.au/internet/healthemergency/publishing.nsf/Content/news-170609 (accessed Sep 2009).
5 Call SA, Vollenweider MA, Hornung CA, et al. Does this patient have influenza? *JAMA* 2005; 293: 987-997.
6 Simonsen L, Fukuda K, Schonberger LB, Cox NJ. The impact of influenza epidemics on hospitalizations. *J Infect Dis* 2000; 181: 831-837.
7 Szewczuk E, Thapa K, Anninos T, et al. Rapid semi-automated quantitative multiplex tandem PCR (MT-PCR) assays for the differential diagnosis of influenza-like illness. *BMC Infect Dis* 2010; 10: 113.
8 International Health Terminology Standards Development Organisation. SNOMED CT. http://www.ihtsdo.org/snomed-ct (accessed Sep 2009).
9 Denholm JT, Gordon CL, Johnson PD, et al. Hospitalised adult patients with pandemic (H1N1) 2009 influenza in Melbourne, Australia. *Med J Aust* 2010; 192: 84-86.
10 ANZIC Influenza Investigators; Webb SA, Pettilä V, Seppelt I, et al. Critical care services and 2009 H1N1 influenza in Australia and New Zealand. *N Engl J Med* 2009; 361: 1925-1934.
11 Nachimuthu SK, Lau LM. Practical issues in using SNOMED CT as a reference terminology. *Stud Health Technol Inform* 2007; 129: 640-644.
12 Lipsitch M, Viboud C. Influenza seasonality: lifting the fog. *Proc Natl Acad Sci U S A* 2009; 106: 3645-3646.
13 Lofgren E, Fefferman NH, Naumov YN, et al. Influenza seasonality: underlying causes and modeling theories. *J Virol* 2007; 81: 5429-5436.
14 Kelly HA, Grant KA, Williams S, et al. Epidemiological characteristics of pandemic influenza H1N1 2009 and seasonal influenza infection. *Med J Aust* 2009; 191: 146-149.
15 Louie JK, Acosta M, Winter K, et al. Factors associated with death or hospitalization due to pandemic 2009 influenza A(H1N1) infection in California. *JAMA* 2009; 302: 1896-1902.
16 Torres J, O'Ryan M, Herve B, et al. Impact of the novel influenza A (H1N1) during the 2009 autumn–winter season in a large hospital setting in Santiago, Chile. *Clin Infect Dis* 2010; 50: 860-868.
17 Bishop JF, Murnane MP, Owen R. Australia's winter with the 2009 pandemic influenza A (H1N1) virus. *N Engl J Med* 2009; 361: 2591-2594.
18 Ikonen N, Strengell M, Kinnunen L, et al. High frequency of cross-reacting antibodies against 2009 pandemic influenza A(H1N1) virus among the elderly in Finland. *Euro Surveill* 2010; 15 (5): pii: 19478.
19 Miller E, Hoschler K, Hardelid P, et al. Incidence of 2009 pandemic influenza A H1N1 infection in England: a cross-sectional serological study. *Lancet* 2010; 375: 1100-1108.
20 Pan C, Cheung B, Tan S, et al. Genomic signature and mutation trend analysis of pandemic (H1N1) 2009 influenza A virus. *PLoS One* 2010; 5: e9549.
21 Ross T, Zimmer S, Burke D, et al. Seroprevalence following the second wave of pandemic 2009 H1N1 influenza. *PLoS Curr Influenza* 2010; Feb 24: RRN1148.
22 Centers for Disease Control and Prevention (CDC). Interim recommendations for clinical use of influenza diagnostic tests during the 2009–10 influenza season. Atlanta: CDC, 2009.
23 van Hal S, Foo H, Blyth C, et al. Influenza outbreak during Sydney World Youth Day 2008: the utility of laboratory testing and case definitions on mass gathering outbreak containment. *PLoS One* 2009; 4: e6620.
24 Muscatello DJ, Churches T, Kaldor J, et al. An automated, broad-based, near real-time public health surveillance system using presentations to hospital Emergency Departments in New South Wales, Australia. *BMC Public Health* 2005; 5: 141.

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