Enhanced surveillance for serious complications of influenza in children: role of the Australian Paediatric Surveillance Unit

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Abstract

Influenza contributes significantly to disease burden among children aged less than five years. Existing influenza surveillance systems do not provide detailed data on clinical presentation, management, vaccination status, risk factors and complications in hospitalised children, or link such data with laboratory results. Following a number of child deaths due to influenza in 2007, the Australian Government Department of Health and Ageing approached the Australian Paediatric Surveillance Unit (APSU) to examine the feasibility of enhancing APSU surveillance to identify children hospitalised with severe complications of influenza. Active, national, weekly surveillance was conducted during September 2007 with reporting by 1,256 Australian paediatricians working in hospitals and outpatient settings. The weekly report card return rate was 93%; detailed clinical data were provided on 88% of all notified cases and 15 children met the case criteria for severe complications of influenza. Admission to hospital occurred within 48 hours of onset of symptoms in over half of the children, of whom 13 had influenza A and two had influenza B, confirmed mostly by polymerase chain reaction on nasopharyngeal aspirate. Serious complications included pneumonia, presumed viral (67%), secondary bacterial infection, shock, cardiomyopathy, myocarditis and hypoglycaemia. No child aged six months or older had been vaccinated against influenza, including three children with underlying chronic conditions. No eligible child received an antiviral agent for influenza. Length of hospital stay ranged from 2 to 34 days; four children were admitted to a Paediatric Intensive Care Unit and one was ventilated. This study demonstrates the feasibility of using the established APSU mechanism for enhanced emergency surveillance during disease outbreaks, emergence or importation. *Commun Dis Intell* 2008;32:71–76.

Keywords: influenza, surveillance, child, diagnosis, immunisation

Introduction

Influenza is a common childhood disease with a wide spectrum of severity from minor respiratory symptoms to severe respiratory illness and life-threatening multi-system complications.[1–9] Significant morbidity and mortality of influenza has been reported in Australian children, with an estimated hospitalisation rate of 82 per 100,000 and death rate of 0.2 per 100,000 children aged less than five years.[10] Of 22 children admitted with complications of influenza to one paediatric intensive care unit (PICU) over a short period in 2003, three died and none had been immunised.[7] Compared with 2006, during the 2007 influenza season there were increased numbers of hospital admissions,[11] including a number of child deaths, attributed to influenza and its complications. In response to this, the Australian Paediatric Surveillance Unit (APSU, www.apsu.org.au) was approached in late August 2007 by the Office for Health Protection, Australian Government Department of Health and Ageing to conduct enhanced surveillance for children aged less than five years, hospitalised with serious complications of influenza. Surveillance commenced 10 days later on 1 September and continued until the end of the month.

Currently, influenza surveillance systems in Australia are based on laboratory reporting and sentinel surveillance for influenza-like illness with reporting by general practitioners and hospital emergency departments.[11,12] They provide the number of confirmed cases, trends over time and geographic distribution, however, limited timely information is available on clinical presentation and risk factors, investigations and hospital management, complications, treatment, and outcomes. A surveillance system able to rapidly provide detailed clinical and laboratory data on children with serious complications of influenza would add value to existing systems. It would enable us to identify clusters of severe disease, diagnostic and management practice, and raise awareness amongst clinicians. Surveillance would inform us of sub-groups at most risk of serious complications and these data would be useful in the development of future immunisation policy and guidelines for diagnosis and treatment of influenza in children.

APSU conducts active, national surveillance for incident cases of rare conditions or rare complications of common conditions in children.[13] Paediatricians and other child health specialists respond to a monthly report card that lists up to 16 different

conditions. The report card, sent by email (68%) or post, is expected to be returned whether a case has been seen or not. Currently, 96% of the monthly report cards sent to 1,256 clinicians (representing approximately 92% of paediatricians practicing in Australia and listed on the Royal Australasian College of Physicians list of Fellows) are returned.[13] Clinicians reporting cases are sent a two-page questionnaire (adapted for each condition) requesting information on the demographics, management and short-term outcomes for the child.

Our aim was to determine whether APSU can provide timely enhanced data during outbreaks, emergence or importation.

Methods

A modified version of the routine APSU surveillance mechanism was used for surveillance of serious complications of influenza. A separate report card, case definition, study protocol and questionnaire was developed and sent by post to all 1,256 clinicians participating in routine APSU surveillance. Each week during the month of September 2007 a separate influenza report card was sent by post or email, reminding clinicians to report newly diagnosed cases. The questionnaire was included as an attachment to the email report card or as a paper copy with the paper card to clinicians who prefer this method. Clinicians reporting a case were encouraged to complete and return the questionnaire directly via facsimile, email or post. In addition, study materials including the case definition, study protocol and questionnaire were made available on the APSU website www.apsu.org.au. To raise awareness of this surveillance study, an item was placed in the weekly email newsletter of the RACP Division of Paediatrics and Child Health. Urgent ethics clearance was obtained from the Human Research Ethics Committee at the Children's Hospital at Westmead.

Case definition

Clinicians were asked to report any child aged less than five years admitted to hospital with laboratory-confirmed influenza and with any of the complications listed in Table 1.

The questionnaire included items about demographics, presenting symptoms, method of diagnosis, investigations, complications, length of stay in hospital and/or PICU, immunisation status, risk factors such as pre-existing chronic conditions; and other factors of public health interest such as recent overseas travel, close contact with farm animals, and contact with other people infected with influenza.

Results

Surveillance results

In September 2007, a total of 5,073 report cards were sent either by email (65%) or surface mail (35%) to practising paediatricians and 4,745 (93%) cards were returned, confirming a high participation rate. There were 4,710 cards received indicating 'nothing to report' and 35 cards reporting a total of

Table 1. Case definition criteria

Any child aged less than five years and admitted to hospital with laboratory confirmed influenza and any of the following complications:

- pneumonia (x-ray confirmed)
- requirement for ventilation
- encephalitis/encephalopathy with or without seizures
- myocarditis; pericarditis; cardiomyopathy
- rhabdomyolysis
- purpura fulminans
- disseminated coagulopathy
- transverse myelitis
- polyneuritis
- Guillain-Barré syndrome
- shock (requiring >40 ml/kg fluid resuscitation)
- acute renal failure
- Reye's syndrome
- laboratory proven secondary bacterial infection; bacteraemia, septicaemia, bacterial pneumonia
- death

Exclusion: simple febrile seizures

58 potential cases of influenza. Questionnaires were completed for 51 of 58 (88%) notifications, allowing for case classification. Of the 51 cases, 15 were confirmed influenza cases, reported from five of the seven Australian states and territories (Table 2). There were 36 reporting errors including four cases that met all case definition criteria but were aged five years or more; 23 cases that did not meet the clinical case definition, most commonly because they had no serious complications; and eight cases were diagnosed outside of the study period, before September 2007 (Table 2).

Demographics and diagnosis

Among the 15 confirmed cases hospitalised with complications of influenza, all were born in Australia, three (20%) identified as Aboriginal or Torres Strait Islander and most (78%) were male. At diagnosis, children ranged in age from 4 days to 3.7 years (median 1.5 years): over half (60%) were aged under two years and three (20%) were aged less than six months. Nasopharyngeal aspirate was the most common sampling method (n=13); a throat swab was taken in one child and the sampling method is not known in the other case. Thirteen children had influenza A and two had influenza B. Influenza was confirmed by polymerase chain reaction in 11 and immunofluorescence in four cases.

Presenting features and complications

The most common symptoms at onset of illness were fever, cough, dyspnoea, and headache. Over half (53%) the children had a rapid clinical deterioration with admission to hospital within 48 hours of the onset of symptoms. Four (27%) children were admitted to a PICU and one child required ventilation (Table 3). The majority of children were seriously ill as indicated by the range of complications (Table 3). The most common complication was x-ray confirmed pneumonia, presumed viral in 10 (67%) children; secondary bacterial pneumonia was identified in only one case (Table 3). Other complications included shock, myocarditis, cardiomyopathy, need for ventilation and hypoglycaemia.

Table 3. Symptoms and signs at onset of illness and complications at presentation to hospital

Symptoms and complications	Confirmed cases (n=15)
Admitted to Intensive Care Unit	4
Symptoms and signs at onset of illness*	
Cough	12
Fever	10
Dyspnea	8
Sore throat	3
Vomiting	2
Headache	5
Stridor	2
Other	3
Complications*	
Pneumonia (presumed viral)	10
Ventilation	1
Shock	1
Secondary infection	
• blood culture +ve for *Moraxella catarrhali*	3
• norovirus and *Clostridium difficile* toxin A isolated from stool	
Hypoglycaemia	2
Cardiomyopathy	1
Dehydration	1

* Some children had more than one symptom or sign and more than one complication.

Table 2. Number of reports and case classification, by state or territory

State	Total notifications	Errors	Questionnaire not returned	Confirmed cases
New South Wales	9	7*	0	2
Northern Territory	–	–	–	–
Queensland	13	9	2	2
South Australia	11	2	3	6
Tasmania	–	–	–	–
Victoria	12	6	2	4
Western Australia	13	12	0	1
Total	58	36	7	15

* One of these notifications was a duplicate report.

Known risk factors, contacts, vaccination status and treatment

Among the 15 confirmed cases, one was a neonate and four had pre-existing chronic conditions, including one child with Down's syndrome, laryngomalacia and hypothyroidism; one 12-week-old infant who was clinically malnourished; one child with congenital heart disease; and one child with asthma.

A contact with laboratory confirmed influenza (a sibling) was identified for only one child. No child had travelled overseas in the 10 days prior to onset of symptoms and no child had close recent contact with pigs, poultry or birds.

None of the 10 children aged six months or older had been vaccinated against influenza, including three children with pre-existing chronic conditions. Only four children had been vaccinated against pneumococcus. None of nine children aged over 12 months and eligible for treatment with the anti-influenza drug Tamiflu™ (oseltamivir phosphate) received the drug.

Outcomes

Admission to hospital occurred within 48 hours of onset of symptoms in over half of children. Length of hospital stay ranged from 2 to 30 days (median 6.5 days). Length of stay in PICU ranged from 3 to 20 days (3 cases). At the time of reporting, 13 of the 15 children hospitalised with complicated influenza had been discharged with no ongoing medical problems. There were no deaths reported. One child remained in PICU for 20 days after admission and one child remained in hospital 34 days after admission and final outcome data are not available for these two children.

Discussion

We have demonstrated that the APSU surveillance system can be modified and mobilised quickly, in the event of an epidemic, to enable enhanced surveillance for diseases of public health interest, such as severe complications of influenza. Within 10 days of being commissioned by the Department of Health and Ageing to undertake this project, we had consulted experts in the field and formed an investigators group; developed a case definition, study protocol, reporting instructions, report card and questionnaire; obtained ethics approval; publicised the study among reporting paediatricians; and begun surveillance.

Our data demonstrate that the 1,256 clinicians who report each month to the APSU are willing to participate in emergency surveillance, for example during an epidemic. This is confirmed by the 93% response rate to the weekly report card and provision of clinical data for 88% of notified cases. Furthermore, the study provided an educational opportunity. At the outset of the study APSU provided all paediatricians with important information about the method of diagnosis, investigation, management and known risk factors for influenza and highlighted the importance of asking about vaccination status, pre-existing conditions and recent overseas travel in children presenting with flu-like symptoms. The data collected were timely, detailed, and nationally representative and clinical and laboratory data could be linked immediately and related to outcomes. Such data are currently not available from any other source. Potentially, such enhanced APSU surveillance could also be used to collect data on new, emerging, or introduced diseases and to inform public health response for disease management and prevention.

Our data highlight a number of important issues for clinicians. Young children who are subsequently hospitalised with complications of influenza present with typical 'flu-like' symptoms but deteriorate quickly (over a half were admitted within 48 hours of onset of symptoms); presumed viral pneumonia is the most common complication; and prognosis is usually excellent. None of the children in our study had been diagnosed before presenting to hospital. None of the children eligible for treatment with oseltamivir had been treated, despite evidence that treatment shortens the duration of illness.[14] Trials of point-of-care testing for influenza in the primary health care setting and in emergency departments, coupled with early treatment using oseltamivir are needed to determine whether such measures will reduce the number of children hospitalised due to influenza and the number of serious complications in children. Such trials may also inform the development of Australian clinical practice guidelines for diagnosis and treatment of children presenting with influenza-like illness.

None of the children in our study, who were eligible for vaccination, had been vaccinated against influenza, including four with pre-existing chronic conditions. Because influenza contributes to a significant disease burden among children, the USA Advisory Committee on Immunization Practices now recommends vaccination for all children aged six months to five years.[15] In 2003, Milne, et al. called for further discussion regarding inclusion of similar recommendations on the Australian Immunisation Schedule.[7] The 2007 *Australian Immunisation Handbook* includes a recommendation for the vaccination of children aged six months or older who are immunocompromised or who have chronic conditions that may predispose them to severe complications of influenza and states that 'influ-

enza vaccine should be administered to any person who wishes to reduce the likelihood of becoming ill with influenza'.[16] However, influenza vaccination for healthy children is not currently funded under the National Immunisation Schedule. Enhanced surveillance data and detailed review of hospital records of children admitted to hospital with laboratory-confirmed influenza will be important to inform changes to immunisation recommendations and to monitor the effectiveness of such changes. We are currently undertaking an audit of all (122) cases of influenza admitted to the Children's Hospital at Westmead in 2007.

Although the number of children identified in this short (one month) surveillance period at the end of the influenza season is small, our data show that children are hospitalised with a range of serious, often multiple, complications of influenza. We cannot compare the reporting rate in our study with data provided by laboratory and sentinel surveillance systems currently operating in Australia, as these existing systems do not provide information about severity of illness and specific complications by age group. The highest burden of influenza admissions is known to be in children aged under two years[10] and this is reflected in our study, in which 60% were aged under two years. However, four additional cases reported among older children but excluded from our analysis illustrate that children aged over five years may also suffer severe multisystem complications. Of the three males and one female (aged 7.5, 7.9, 9.4 and 13.7 years), three were admitted to PICU and two required ventilation (for 5 days and 11 days). Three had influenza A and one had influenza B. Their complications included pneumonia, encephalopathy, disseminated coagulopathy, seizure, shock, Reye's syndrome and acute necrotising encephalopathy. One of these children had cystic fibrosis; the other three were previously healthy. None had been vaccinated against influenza and two were treated with oseltamivir. These data suggest that future surveillance studies should include children up to the age of 15 years.

With the support of the Department of Health and Ageing we are currently piloting a new Paediatric Active Enhanced Disease Surveillance (PAEDS) system in four major paediatric hospitals in four states (Princess Margaret Hospital for Children in Perth, Women's and Children's Hospital in Adelaide, Royal Children's Hospital in Melbourne and the Children's Hospital at Westmead in Sydney). This hospital based surveillance system involves active case identification by specialist nurses and is modelled on the IMPACT system developed in Canada.[17] The strength of PAEDS lies in its ability to facilitate collection of timely, detailed clinical data in addition to biological specimens. PAEDS, is a collaboration between the APSU and the National Centre for Immunisation Research and Surveillance for Vaccine Preventable Diseases. If sucessfully rolled out to all major paediatric centres around Australia, PAEDS could offer an additional complementary source of ascertaining hospitalised cases of severe complications of influenza.

Conclusions and recommendations

We have demonstrated the potential for using the APSU for emergency surveillance of uncommon conditions. This surveillance system has the advantage of being well established, cheap and enabling linkage of and timely access to epidemiological, clinical and virological data. With an extended period of surveillance (June to September) APSU and/or PAEDS could in future provide prospective enhanced data on hospitalised cases of severe seasonal influenza in Australian children aged under 15 years.

Acknowledgements

We acknowledge all clinicians contributing data to the Australian Paediatric Surveillance Unit, including the Australian and New Zealand Paediatric Intensive Care Units. The APSU is a Unit of the Division of Paediatrics and Child Health, Royal Australasian College of Physicians and is funded by the Australian Government Department of Health and Ageing, the Faculty of Medicine at the University of Sydney, and a National Health and Medical Research Council (NHMRC) Enabling Grant (402784). Elizabeth Elliott is supported by an NHMRC Practitioner Fellowship (457084).

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