

Pediatric influenza-associated myositis – Nebraska, 2001–2007

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Objective Influenza-associated myositis (IAM), characterized by severe lower-extremity myalgia and reluctance to walk, is a complication of influenza among children. We investigated IAM in Nebraska during six influenza seasons, 2001–2007.

Methods During 2006–2007, we requested reports of severe influenza illness among persons aged <18 years and investigated medical records to identify and confirm IAM cases defined as severe myalgia with elevated serum creatinine kinase level in a patient aged <18 years, occurring within 7 days of laboratory confirmed influenza illness onset. Statewide hospital discharge data (HDD) were reviewed to identify retrospectively confirmed IAM cases during 2006–2007 and five previous seasons, by using surveillance data to define periods of influenza activity. Statewide IAM incidence was estimated for 2001–2002 through 2006–2007.

Results During 2006–2007, a total of 13 IAM cases were confirmed by enhanced surveillance. Median age was 6 years

(range, 4–11 years). Influenza diagnosis was established by viral isolation from six patients (one influenza A and five influenza B) and rapid diagnostic tests for seven. Twelve (92%) patients, including one who died, were hospitalized for a median of 3 days (range, 1–4 days). Review of HDD identified 12 retrospectively confirmed IAM cases during 2006–2007, including four not reported through enhanced surveillance, and only one during five previous seasons (2003–2004). The HDD-derived, retrospectively confirmed statewide IAM incidence estimates/1 000 000 population aged <18 years were 2.693 and 0.225 during 2006–2007 and 2003–2004, respectively.

Conclusion An IAM epidemic occurred in Nebraska during the 2006–2007 influenza season.

Keywords Epidemiology, influenza, myositis, rhabdomyolysis, pediatrics.

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Introduction

Influenza is a common childhood disease, usually characterized by acute, self-limited respiratory-tract illness, with attack rates during annual seasonal epidemics that can exceed 40% among preschool and 30% among school-age children.¹ The majority of influenza virus infections result in uncomplicated illness, with fever, cough, and upper-respiratory symptoms. Less commonly, influenza is associated with severe, complicated illness.² In the United States, an estimated annual average of >2 000 000 hospitalizations are attributable to influenza among persons of all ages, and rates of hospitalization among young children are similar to those among adults at high risk for complications.^{1–4} One study estimated that four influenza-related excess hospitalizations per 10 000 children aged 5–14 years occur annually in the United States.¹ Although not represented in

some studies of influenza-associated hospitalizations, one severe but infrequent complication of influenza among school-age children who might require hospitalization is influenza-associated myositis (IAM).⁵ Since first described in 1957,⁶ IAM has been reported sporadically. Children are more frequently affected than adults, and IAM is often associated with influenza B.^{5–23}

In February 2007, the Nebraska Department of Health and Human Services (NDHHS) received notification of a fatal case of illness associated with laboratory-confirmed influenza in a previously healthy girl who had experienced fever, myositis, severe myalgia, septic shock, and pneumonia. This case was published by local media, which prompted reporting of four additional patients hospitalized in Nebraska for illnesses consistent with IAM. In response, NDHHS initiated enhanced surveillance to identify severe, atypical manifestations of influenza among Nebraska

residents aged <18 years, including IAM. Previously, only fatal influenza-associated illnesses were reportable; whether IAM cases had occurred among surviving patients was unknown. Therefore, we conducted a three-part epidemiologic investigation to identify IAM cases in Nebraska by using enhanced surveillance during the 2006–2007 influenza season and to describe clinical features (Part 1); to retrospectively compare 2006–2007 IAM incidence with the five preceding influenza seasons, 2001–2006 (Part 2); and to estimate total 2006–2007 IAM incidence by capture–recapture methodology (Part 3).

Methods

Part 1: Health department enhanced surveillance – influenza season 2006–2007

Enhanced surveillance was initiated by NDHHS to identify IAM cases. A Health Alert Network (HAN) message was sent to Nebraska physicians, hospital infection control and prevention staff, and local health department personnel on February 16, 2007, to request reports of severe and atypical manifestations of laboratory-confirmed influenza among persons aged <18 years, occurring on or after January 1, 2007. During the 2006–2007 influenza season, routine statewide surveillance data indicated that influenza virus activity was negligible before January 2007 (NDHHS 2006–2007, unpublished data). An online form was used by hospital infection control and prevention staff or local health department personnel to report potential IAM cases to NDHHS. For reported patients, we collected additional information by review of medical records and by parent or guardian interviews.

A confirmed IAM case was defined as severe myalgia with elevated serum creatinine kinase (CK) level (>2 times upper limit of normal range) occurring within 7 days of laboratory-confirmed influenza illness onset on or after January 1, 2007, in a patient aged <18 years who had been examined in an emergency department or who had been hospitalized. Laboratory confirmation of influenza was established by a positive influenza result on testing of upper-respiratory-tract clinical specimens by any of the following: rapid influenza diagnostic test, immunofluorescence, reverse transcriptase-polymerase chain reaction, or viral culture.

Part 2: Estimated IAM incidence by retrospective hospital discharge data review – influenza seasons 2001–2002 through 2006–2007

To retrospectively estimate and compare IAM incidence during each of the six influenza seasons during 2001–2007, we reviewed Nebraska hospital discharge data, which include deidentified inpatient and emergency department discharge records from all Nebraska acute-care, non-federal

hospitals. These data contain up to 10 *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) diagnosis codes. To define periods of influenza activity, we used influenza data reported from the U.S. West North Central Region by the World Health Organization and National Respiratory and Enteric Virus Surveillance System (WHO/NREVSS) collaborating laboratories (Table 1).^{24–29} Regional data were used because statewide influenza surveillance was initiated after influenza season 2002–2003 and Nebraska-specific data were unavailable for influenza seasons before 2003–2004.

To retrospectively identify confirmed and probable IAM cases, we first selected all records with ICD-9-CM coding of influenza (487.0, influenza with pneumonia; 487.1, influenza with other respiratory manifestations; or 487.8, influenza with other manifestations) from Nebraska hospital discharge data records of persons aged <18 years with admission during the six previously defined 2001–2007 influenza seasons (Table 1). Among these records, we then identified records with concurrent ICD-9-CM coding to indicate at least one muscle disorder consistent with myositis (Box 1). Records identified by this search strategy were temporarily considered potential IAM cases and were then further defined as retrospectively confirmed or probable, or excluded. We collaborated with the Nebraska Hospital Association and member hospitals to locate and review these medical records. A retrospectively confirmed IAM case was defined as severe myalgia with elevated serum CK level (>2 times upper limit of normal range) in an

Table 1. Influenza activity date ranges and corresponding number of influenza season weeks during six consecutive influenza seasons – Nebraska, 2001–2007

Influenza season	Influenza activity date range*	No of influenza season weeks
2001–2002	Jan. 6, 2002–May 18, 2002	19
2002–2003	Dec. 22, 2002–May 3, 2003	19
2003–2004	Nov. 9, 2003–March 6, 2004	17
2004–2005	Dec. 12, 2004–April 23, 2005	19
2005–2006	Dec. 18, 2005–April 22, 2006	18
2006–2007	Dec. 10, 2006–April 14, 2007	18

*Influenza activity date range includes the weeks during each influenza season when the proportion of specimens testing positive for influenza first exceeded 5%, all weeks that exceeded 5%, and the week when proportion of positives declined below 5% as reported from the U.S. West North Central Region by World Health Organization and National Respiratory and Enteric Virus Surveillance System (WHO/NREVSS) collaborating laboratories.^{24–29}

Box 1. Criteria for selection of potential influenza-associated myositis (IAM) cases for subsequent identification as probable or retrospectively confirmed cases – Nebraska, 2001–2007

Potential IAM case

Nebraska hospital discharge data record
Admission date during six previously defined influenza seasons (2001–2007)*
Aged <18 years
At least one ICD-9-CM code from both group A and group B

Group A

487-0, Influenza with pneumonia
487-1, Influenza with other respiratory manifestations
487-8, Influenza

Group B

728-88, Rhabdomyolysis
728-0, Infective myositis
728-9, Unspecified disorder of muscle, ligament, and fascia
728-89, Other disorder of muscle, ligament, and fascia
729-1, Myalgia and myositis, unspecified
729-5, Pain in limb
729-89, Other musculoskeletal symptoms referable to limbs
729-9, Other and unspecified disorders of soft tissue
710-4, Polymyositis
791-3, Myoglobinuria

ICD-9-CM, *International Classification of Diseases, Ninth Revision, Clinical Modification*.

*Refer to Table 1.

inpatient or emergency department patient aged <18 years occurring within 7 days of laboratory-confirmed influenza illness during the defined 2001–2002 through 2006–2007 influenza seasons (Table 1). A probable IAM case met the same ICD-9-CM coding criteria as retrospectively confirmed cases but lacked laboratory confirmation of influenza or elevated serum CK level or both.

We also searched the same hospital discharge data records by using a separate and different strategy to identify other possible IAM cases, including those possibly managed conservatively in emergency departments that might have occurred among patients without laboratory confirmed or ICD-9-CM-coded influenza during the same study period. A suspect case was defined as a Nebraska hospital discharge data record from a patient aged <18 years with admission during the six previously defined influenza seasons (Table 1) with at least one of the following primary ICD-9-CM codes or code combinations: 728-88, rhabdomyolysis (without ICD-9-CM V- or E-codes indicating injury or trauma); 079-99, unspecified viral infection plus a muscle disorder code (Group B, refer to Box 1); or 729-1, myalgia and myositis, unspecified plus 079-99, unspecified viral infection. Chart review of suspect IAM cases was not performed. We calculated the estimated incidence of retrospectively confirmed, probable, and separately identified suspect IAM cases/1 00 000 population

aged <18 years per influenza season and per season week by using the 2-year averages of U.S. Census Bureau yearly estimates of Nebraska's population aged <18 years for the respective influenza season years as the denominators.³⁰ For example, for influenza season 2001–2002, we averaged 2001 and 2002 population estimates.

Part 3: Estimated IAM incidence by capture–recapture analysis – influenza season 2006–2007

To estimate the total number of confirmed IAM cases that occurred during influenza season 2006–2007, we performed capture–recapture analysis comparing all confirmed cases identified by both enhanced surveillance and retrospective hospital discharge data review.^{31–33} With the resulting point estimate and the previously established population denominator, we calculated 2006–2007 confirmed IAM incidence/1 00 000 population aged <18 years.

Human subjects review

This investigation underwent Centers for Disease Control and Prevention human subjects review and was determined to be public health practice and not research; as such, Institutional Review Board approval was not required.

Results

Part 1: Health department enhanced surveillance – influenza season 2006–2007

Of 17 patients aged <18 years reported to NDHHS during influenza season 2006–2007 enhanced surveillance, four failed to meet the confirmed IAM case definition and were excluded, and 13 experienced illness that met the confirmed IAM case definition. Of these, six were admitted to one children's hospital, and the other seven were reported from six different hospitals. Eight resided in Nebraska's two largest cities (Omaha and Lincoln), and five lived in geographically dispersed locations. 10 (77%) were male, three (23%) were female, and the median age was 6 years (range, 4–11 years). Twelve (92%) of 13 patients were hospitalized; one (8%) was not admitted but required emergency department visits on four consecutive days. For the 12 inpatients, the median length of hospitalization was 3 days (range, 1–4 days). A female aged 11 years who experienced IAM, septic shock, pneumonia, and cardiopulmonary failure required intensive care and mechanical ventilation, and had rapid clinical progression to death. She had been hospitalized twice for dehydration in the prior year but had not been diagnosed with any underlying medical conditions.

Of 13 confirmed IAM patients, three without high-risk conditions had been administered influenza vaccine during 2006–2007 at least 2 weeks before onset of influenza illness. Of 10 unvaccinated children, six did not have a high-risk

condition for which influenza vaccine is recommended, including the child who died, and four had high-risk conditions recommended for annual influenza vaccination (three had asthma/reactive airway disease, and one was aged <5 years).

The chief complaint at admission for all 13 patients was severe myalgia. Median duration of onset from influenza illness to muscle pain was 5 days (range, 2–7 days). Illness onset ranged from February 6 to March 5, 2007. All 13 experienced acute, severe bilateral calf pain; 12 (92%) were unable to walk; and four (31%) were unable to stand. Other manifestations included crawling instead of walking (15%), wide-based stance (15%), and standing on toes (8%). Four experienced pain in other muscle groups (three experienced neck pain, low back pain, or bilateral thigh pain, and one experienced bilateral, generalized thigh, hamstring, and foot pain). Among 12 inpatients for whom clinical data were available, five (42%) reported complete,

and seven (58%) reported partial resolution of respiratory symptoms before onset of muscle pain.

Three of 13 patients experienced elevated temperatures ranging from 100.7°F to 103.0°F documented during admission or from emergency department records. Laboratory data are presented in Table 2. No neurologic deficits were identified in any patients. Rhabdomyolysis was diagnosed in five patients (42%), and two (15%) had experienced myoglobinuria, including the patient who died (peak CK = 52 999 U/l, peak myoglobin = 9020 ng/ml).

Of the 12 surviving patients, parents or guardians of 11 (92%) were interviewed. Of these, seven reported resolution of myositis symptoms at discharge. Four patients, including the emergency department-discharged patient, reported incomplete improvement at discharge. For these, the median time from discharge to complete resolution was 4.5 days (range, 3–60 days). A female aged 9 years who was hospitalized for 4 days was unable to walk at discharge and experienced muscle pain for 60 days.

Viral analyses and antigenic characterization of six isolates (five from unvaccinated patients) were performed by the Centers for Disease Control and Prevention, Atlanta, Georgia (Table 3). A/New Caledonia/20/99-like (H1N1) virus (the H1N1 vaccine strain) was isolated from the unvaccinated patient who died. B/Florida/07/2004-like virus (distinct lineage from the vaccine strain B/Ohio/1/2005-like) was isolated from a previously healthy male aged 6 years who had been administered live-attenuated influenza virus vaccine 4 months earlier.

Part 2: Estimated IAM incidence by retrospective hospital discharge data review – influenza seasons 2001–2002 through 2006–2007

From Nebraska hospital discharge data, 5826 influenza cases were retrospectively identified among patients aged <18 years from the beginning of the 2001–2002 season through the end of the 2006–2007 season (Figure 1); 15.1% (878/5826) were inpatients. During 2006–2007, a total of 32 potential IAM cases were identified and subsequently further defined. Of these, 12 met the retrospectively

Table 2. Laboratory findings for 13 patients with confirmed influenza-associated myositis (IAM) identified by enhanced surveillance – Nebraska, 2006–07 influenza season

Parameter	Surviving confirmed IAM cases (n = 12)			Non-surviving case values (n = 1)
	No of patients with reported values	Median value	Range	
WBC count (per μ l)				
Nadir/patient	11	3.00	2.40–5.19	12.32
Peak/patient	11	3.83	2.40–12.30	21.67
Peak CK (U/l)	12	2963	442–13 426	52 999
AST (U/l)	5	105	50–405	516
ALT (U/l)	6	68	36–123	96
Creatinine (mg/dl)	12	0.5	0.2–0.8	1.0
BUN (mg/dl)	12	11	7–17	16
Myoglobin (ng/ml)	10	772	73–3278	9020
Hemoglobin (g/dl)	11	14	12.2–14.4	17.0

Influenza virus	No (%)	Commercial rapid test	Viral culture	Viral antigenic characterization
Type B	9 (69.2)	4	5	B/OHIO/01/2005-LIKE (n = 4) B/FLORIDA/07/2004-LIKE (n = 1)
Type A	2 (15.4)	1	1	A/NEW CALEDONIA/20/99-LIKE (H1N1)
A/B not distinguished	2 (15.4)	2	0	NA

NA, not applicable.

Table 3. Diagnostic findings for detection of influenza viruses among 13 patients with confirmed influenza-associated myositis (IAM) identified by enhanced surveillance – Nebraska, 2006–2007 influenza season

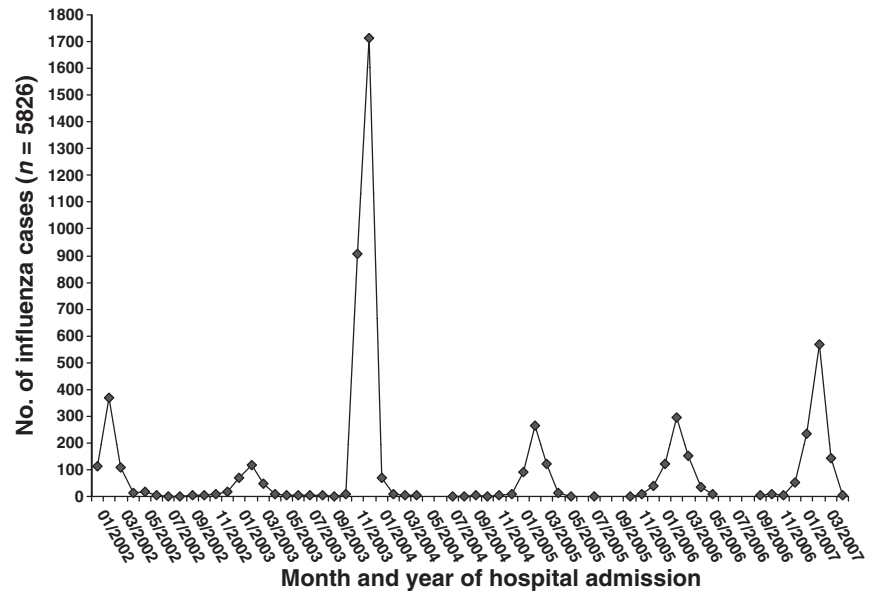


Figure 1. Number of influenza cases retrospectively identified from review of hospital discharge records of patients aged <18 years, by month and year of admission – Nebraska, influenza seasons 2001–2002* through 2006–2007.

*For the 2001–02 influenza season, 2001 records not evaluated because surveillance data indicated low influenza activity before January 2002 (Table 1).²⁴

confirmed IAM case definition – eight were previously identified by enhanced surveillance (Part 1) and the other four previously healthy patients were only identified by retrospective case finding. Of the 20 remaining potential cases, 11 were excluded for failing to meet case definitions and nine met the probable case definition after chart review. Table 4 lists clinical characteristics of four retrospectively confirmed IAM cases that were not captured by 2006–2007 enhanced surveillance and nine probable cases, of which five (55.6%) were emergency department-discharged. During influenza season 2006–2007, estimated statewide incidence of retrospectively confirmed IAM was 2.693 cases/1 000 000 population aged <18 years.

During the 2001–2002 through 2005–2006 influenza seasons, nine potential IAM cases were retrospectively identified and subsequently further defined. Of these, only one met the retrospectively confirmed IAM case definition – a male aged 7 years who had been admitted on November 20, 2003, and hospitalized 2 days for bilateral calf pain and inability to walk. A rapid influenza test was positive for type A, and serum CK was 11 696 U/l. During the 2003–2004 influenza season, estimated statewide incidence of retrospectively confirmed IAM was 0.225 cases/1 000 000 population aged <18 years. Of eight remaining potential IAM cases identified and further defined during the same seasons, six were excluded and two emergency department discharges met the probable case definition after chart review. Table 5 lists the retrospectively established statewide incidence estimates of retrospectively confirmed, probable, and separately identified suspect IAM cases during 2001–2007.

Table 4. Clinical and laboratory findings and demographic information for 13 patients with retrospectively confirmed* and probable influenza-associated myositis (IAM) identified only by retrospective review of hospital discharge data – Nebraska, 2006–2007 influenza season

Parameter	Case classification	
	Retrospectively confirmed*	Probable
Total, <i>n</i>	4	9
Median age, years	9	7
Range, years	7–14	4–12
Sex		
Male, <i>n</i> (%)	2 (50.0)	7 (77.8)
Female, <i>n</i> (%)	2 (50.0)	2 (22.2)
Elevated CK, <i>n</i> (%)	4 (100.0) [†]	5 (55.6)
Range (U/l)	869–6053	221–15 225
Positive influenza test result, <i>n</i> (%)	4 (100.0) [‡]	3 (33.3)
Type A, <i>n</i>	1	0
Type B, <i>n</i>	3	2
A/B not distinguished, <i>n</i>	0	1
Admission date (range)	2/14/2007–3/19/2007	2/14/2007–3/31/2007
Hospitalized, <i>n</i> (%)	3 (75.0)	4 (44.4)

*Eight patients with retrospectively confirmed IAM not included because previously described in Part 1 of investigation.

[†]Elevated creatinine kinase (CK) required to meet retrospectively confirmed case definition.

[‡]Positive influenza test result required to meet retrospectively confirmed case definition.

Table 5. Number of retrospectively confirmed, probable, and suspect influenza-associated myositis (IAM) cases identified only by retrospective review of hospital discharge data and corresponding estimated incidence during six consecutive influenza seasons – Nebraska, 2001–2007

Influenza season	Confirmed* (n)	Probable (n)	Suspect (n)	State population aged <18 years†	IAM incidence/1 00 000 population aged <18 years					
					Confirmed*		Probable		Suspect	
					Season	Season week	Season	Season week	Season	Season week
2001–2002	0	0	6	4 46 729	0	0	0	0	1.343	0.0707
2002–2003	0	1	5	4 45 759	0	0	0.224	0.0118	1.122	0.0590
2003–2004	1	1	4	4 45 408	0.225	0.0132	0.225	0.0132	0.898	0.0528
2004–2005	0	0	4	4 45 179	0	0	0	0	0.899	0.0473
2005–2006	0	0	6	4 45 003	0	0	0	0	1.348	0.0749
2006–2007	12	9	28	4 45 620	2.693	0.1496	2.020	0.1122	6.283	0.3491

*Retrospectively confirmed.

†All influenza season incidence calculations use a 2-year population average.³⁰

Part 3: Estimated IAM incidence by capture–recapture analysis – influenza season 2006–2007

When capture–recapture analysis was applied to the 17 total confirmed IAM cases identified during the 2006–2007 influenza season (five only by enhanced surveillance, four only by retrospective case finding, and eight by both methods), the point estimate for the actual number of confirmed IAM cases statewide (Table 6) was calculated as 19.5 (95% confidence interval [CI] 14.7–24.3), corresponding to an estimated confirmed IAM incidence of 4.376 cases/1 00 000 population aged <18 years (95% CI 3.290–5.462).

Table 6. Capture–recapture* estimate of overall statewide number of patients with confirmed influenza-associated myositis (IAM) – Nebraska, 2006–2007 influenza season

	Retrospective case finding (Part 2 of investigation)		
	Identified	Missed	
Enhanced surveillance (Part 1 of investigation)	Identified 8 (a = m2)	5 (b)	13
	Missed 4 (c)	2.5 (z)†	(n2 = a + b)
	12 (n1 = a + c)		
	Peterson estimate* of N = 19.5 (95% CI 14.7–24.3) = (n1 × n2)/m2		

*Capture–recapture methodology described elsewhere.^{31–33}

†z = estimated number of confirmed cases missed by both systems = (b × c)/a.

Discussion

This is the first report of IAM that used population-based, statewide data and capture–recapture methods to estimate incidence. All 17 confirmed IAM cases identified by either of the combined surveillance methods (Part 1, enhanced; Part 2, retrospective) occurred during an 8-week period of the 18-week 2006–2007 season. Approximately 20 overall 2006–2007 confirmed IAM cases were estimated by capture–recapture, and the corresponding incidence estimate was 4.376 cases/1 00 000 population aged <18 years. On the basis of hospital discharge data record review that allowed direct comparison between seasons, statewide retrospectively confirmed IAM incidence/1 00 000 population aged <18 years in 2006–2007 (2.693) was approximately 12 times higher than that estimated during 2003–2004 (0.225), the only one of five preceding influenza seasons in which a single retrospectively confirmed IAM case was identified. Additionally, 2006–2007 incidence estimates of probable cases and separately identified suspect IAM cases, likely including cases managed more conservatively, were approximately nine and five times greater, respectively, than the next highest influenza season estimates.

The characteristics of the 17 confirmed IAM cases we identified are consistent with others reported in the medical literature.^{5–23} Pediatric myositis was first described in 1957 by Lundberg as myalgia cruris epidemica among 70 children and four adults who had experienced muscle pain associated with influenza-like prodromal symptoms suggesting a viral etiology.⁶ In 1970, Middleton *et al.* described 26 cases with elevated serum CK concentrations associated with influenza virus infection.⁸ Influenza-associated myositis typically occurs with a 2:1 male predominance among children aged ≤14 years and is characterized by abrupt

onset of severe myalgia in calf muscles, inability to walk, and elevated serum CK levels, usually within 1 week of influenza onset, when respiratory symptoms are improving.⁵ Of 17 Nebraska patients with confirmed IAM in 2006–2007, 13 were previously healthy, including the patient who died; 12 (71%) were male, with a median age of 8 years (range, 4–14 years). Fifteen (88%) required hospitalization and all experienced severe, bilateral calf pain and substantially elevated serum CK levels. Of the 13 identified by enhanced surveillance, all except one were unable to walk, and myositis occurred a median of 5 days after onset of influenza illness, when respiratory symptoms had resolved or were improving. Whereas the link between influenza and IAM is clearly established, the pathogenesis resulting in myositis is not well-understood. Two proposed mechanisms suggest viral invasion of muscle tissue or immune-mediated muscle damage triggered by respiratory-tract virus infection.⁵

During 2006–2007, a total of 80% (12/15) of confirmed IAM patients with available influenza type results were infected with influenza B viruses. Of six patients from whom viral isolates had been characterized antigenically, five (four influenza B and one A/H1N1) had not been vaccinated and were infected with strains similar to corresponding 2006–2007 influenza-vaccine strains, suggesting this illness complex might have been prevented by vaccination. One child to whom vaccine was administered was infected with an influenza B virus strain that was of different lineage and antigenically distinct from the B vaccine strain. Two other vaccinated patients were infected, but viral isolates were not available for strain characterization.

The level of influenza B activity in Nebraska during the 2006–2007 season was apparently higher compared with levels in surrounding states during this same season and compared with levels during previous seasons in Nebraska. According to Nebraska surveillance data, influenza B accounted for 29.9% of positive tests during 2006–2007 compared with 16.1% and 13.7% during 2004–2005 and 2005–2006, respectively (NDHHS, unpublished data). Regional data did not demonstrate a similar trend. According to data reported from the U.S. West North Central Region by the World Health Organization and National Respiratory and Enteric Virus Surveillance System (WHO/NREVSS) collaborating laboratories, influenza B only accounted for 16.2% of positive tests during 2006–2007, a level approximately half that observed in Nebraska and substantially lower than the regional levels observed during the two preceding seasons (20.6%, 2004–2005; 26.7%, 2005–2006).^{27–29}

The number of IAM cases identified and proportion hospitalized during 2006–2007 were substantially higher, compared with the five preceding influenza seasons (2001–2006). One possible contributing factor is that awareness of

a pediatric IAM case associated with fatal influenza-associated illness occurring in February 2007 might have influenced clinical management of IAM patients. This patient's illness occurred before that of any of the other 16 confirmed IAM cases identified through enhanced or retrospective surveillance. Media attention focusing on the fatal case might have resulted in an increase in influenza testing, thus leading to identification of more confirmed IAM cases during 2006–2007. Additionally, parents who were aware of the fatal case might have requested influenza testing and hospitalization for any children experiencing IAM-like symptoms. For these reasons, a proportion of the hospitalized cases that we report might otherwise have been managed more conservatively, possibly in private practice settings and thus would not have been identified as confirmed cases through our surveillance methods.

Our findings are subject to certain limitations. We restricted 2006–2007 enhanced surveillance case finding to laboratory-confirmed influenza cases among hospitalized patients or those presenting to emergency departments. Therefore, any IAM patients treated in hospital settings but without laboratory confirmation of influenza were not captured, including patients with false-negative test results. Those treated in primary-care, non-hospital settings were also missed, even if influenza was laboratory confirmed. Furthermore, patients treated in the limited number of Nebraska hospitals that do not report hospital discharge data would not have been identified retrospectively (Part 2) and the two surveillance systems might not have been completely independent. For all these reasons, we likely underestimated true incidence of IAM in Nebraska during 2006–2007. Because statewide influenza surveillance data were not available for all six 2001–2007 influenza seasons, we used regional rather than Nebraska influenza surveillance data to identify weeks of influenza activity. Accordingly, we might have missed IAM cases occurring at the beginning or end of the influenza seasons when activity was low. Finally, lack of any specific ICD-9-CM code for IAM precluded verification or exclusion of cases defined as suspect.

These results demonstrate that a substantial increase in the number of pediatric IAM cases occurred among Nebraska residents during the 2006–2007 influenza season, an epidemic compared with five previous seasons. Pediatricians and emergency department physicians should include IAM in the differential diagnosis of illness in a child aged <18 years experiencing abrupt onset of severe, lower-extremity myalgia, reluctance or inability to walk, and normal neurologic findings, particularly when symptoms follow influenza or influenza-like illness. Elevated serum CK concentrations and influenza testing on upper-respiratory specimens help establish a diagnosis of IAM. Early recognition of IAM is indicated to monitor for occurrence of rhabdomyolysis and for aggressive treatment of

associated complications (e.g., metabolic abnormalities, myoglobinuria, compartment syndrome, and renal failure).⁵ Most of the patients in this series, particularly those with indication for vaccination, represent missed opportunities to prevent influenza. If the recommendation for annual influenza vaccination of persons aged 6 months–18 years^{34,35} results in high vaccine coverage among school-age children, a reduction in influenza and associated complications such as IAM might occur in this age-group.

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Author's note

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