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Medically attended pediatric influenza during the resurgence of the Victoria lineage of influenza B virus

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Summary
Objectives: During the 2002—2003 season, a new variant of influenza B co-circulated with influenza A viruses. This study examines the characteristics and outcomes of children with influenza A and B virus infection vs. other acute respiratory illnesses.
Methods: A retrospective chart review was performed on children with laboratory-confirmed influenza infection, and influenza negative acute respiratory illnesses that prompted a hospital visit.
Results: Children with influenza were more often previously healthy and presenting with upper respiratory symptoms, while influenza negative patients typically had underlying medical conditions, and lower respiratory tract disease. Children with influenza B were older, were more likely to be in school, and presented with myositis more frequently than those with influenza A. A third of children with influenza A, and 42% with influenza B required hospitalization. The highest hospitalization rates were in infants under one year. No healthy children, and only 15% of those with chronic medical problems, had received influenza vaccine. Vaccine efficacy was estimated to be 82.6%.
Conclusions: Most children with influenza were previously healthy. Overall, a third of children with influenza required hospitalization. Influenza A and B were clinically indistinguishable, except for older age and higher incidence of myositis in patients with influenza B. Influenza vaccine coverage in both healthy and high-risk children was low.

Introduction

Influenza is a common childhood disease with attack rates as high as 30—48% in preschool and school-aged children during epidemics.[1—3] Influenza accounts for significant morbidity and mortality each year, especially in patients with chronic medical conditions and at the extremes of the age spectrum.[1,4,5] Influenza has also been associated with increased incidence of acute otitis media, secondary bacterial pneumonia, and febrile seizures.[6—8] Antibiotic prescriptions for children are estimated to increase by 10—30% during the winter months due to influenza and its complications.[1] Deaths due to influenza are more common in the elderly

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than in children; however, the childhood fatality rate has been estimated to be between 0.7 to 3.8 per 100 000.[4,9] Rates of excess hospitalizations in children associated with influenza have varied between studies, ranging from 4 to 104 per 10 000. Hospitalization rates are consistently higher in patients under 24 months of age.[1,10,11]

In Houston, Texas, a herald outbreak of influenza B appeared at the end of the 2001—2002 winter season with evidence of re-emergence of the Victoria lineage,[12] which last circulated in Houston in 1991. The Yamagata lineage of the B virus circulated in the interim; therefore, children less than 12 years of age had never been exposed to this virus variant. Not much is written in the literature about the differences in the clinical presentations of influenza A and B, other than the association of influenza B and encephalitis[13] and possibly pneumonia[14]. A recent study suggested that children with influenza B are older, and appear less ill than those with influenza A. This study also reported a higher incidence of myalgias and myositis with influenza B.[15]

This descriptive study was designed to examine the characteristics, frequency, and severity of influenza A as compared to influenza B and other viral syndromes in children seeking medical attention in the hospital emergency department and clinics. In addition we estimated hospitalization rates for influenza and immunization rates in healthy and high-risk patient populations.

Methods

Population and study period

Texas Children's Hospital (TCH) is the largest pediatric tertiary care hospital serving the city of Houston and surrounding counties. The TCH Diagnostic Virology Laboratory maintains surveillance of the local activity of influenza viruses by keeping records of all cases of influenza identified in clinical specimens submitted throughout the season. Data were collected from children evaluated for possible influenza A or B infection at TCH between December 1, 2002 and April 30, 2003. The study period included all the influenza-positive specimens for the 2002—2003 winter season.

All children between the ages of 0 and 18 years, who had samples sent from any inpatient or outpatient setting for the diagnosis of influenza during this period, were considered eligible subjects. Tests were ordered during routine ambulatory care, emergency room visits, or inpatient hospital stays by the physicians caring for these patients, as they considered necessary.

Patients with laboratory-confirmed influenza by either positive rapid tests or positive viral cultures were included as study cases. Patients who had a specimen submitted based on the clinical suspicion of influenza by the treating physician (influenza-like illness) and who were influenza negative by laboratory testing were considered for comparison. From this group of influenza-negative patients, one age-matched patient who presented with an influenza-like syndrome within the same week was selected as a control for each influenza-positive patient. A week was defined as the period between Sunday to Saturday to conform to the weekly numbering from the Centers for Disease Control and Prevention (CDC). There were no patients in the neonatal intensive care unit with laboratory-confirmed influenza; therefore, infants in the neonatal unit with negative tests were excluded from the influenza negative comparison group.

Texas Children's Diagnostic Virology Laboratory used the Directigen Flu A/B (Becton—Dickinson Diagnostic Systems, Sparks, MD, USA) test for rapid identification by membrane enzyme immunoassay of viral antigens on all test samples received. A sample of respiratory secretions was obtained by nasal wash performed by nurses, respiratory therapists, or physicians. From every specimen for which a rapid influenza test was requested, a viral tissue culture was also performed by previously described standard methods.[16] The study was reviewed and approved by the Baylor College of Medicine and Affiliated Hospitals institutional review board.

Demographic and clinical characteristics

Demographic and clinical data were collected by retrospective chart review using a standardized form.[16] The information collected for each subject included: age, gender, ethnicity (white, black, Hispanic, or other), source of insurance (none, medicaid, private), and health status (presence or absence of at least one chronic underlying condition including: prematurity, cardiac or pulmonary disease, neuromuscular disease, immunodeficiency, malignancy, transplant, immunotherapy, and significant congenital anomalies).

To compare the severity of illness, a previously used hierarchy was followed.[16] Lower respiratory infection (LRI) (laryngotracheobronchitis, bronchiolitis, and pneumonia as diagnosed by the treating physician) was considered the most severe. Otitis media or sinusitis was the second most severe, and upper respiratory infection (URI) the least severe. We assigned each patient's disease to one of these categories. There were some patients in each group who presented only with vomiting, and although this can be part of an influenza illness, it is not typically the sole presenting symptom. Therefore, these patients with no symptoms other than vomiting were placed in a separate group for the severity of illness tables. The need for oxygen, non-invasive ventilation or mechanical ventilation, death, need of hospitalization, length of stay, and occurrence of a secondary bacterial infection were also recorded. Data on the influenza vaccination status of the patient or the patient's mother during pregnancy, for infants less than six months of age, was collected when available in the medical chart or electronic records at Texas Children's Hospital. Emergency room physicians and hospital house staff were sent monthly reminders during the influenza season to document the influenza immunization history of all patients with influenza-like illnesses. Presenting symptoms, length of illness (at time of presentation), viral and bacterial culture results, and prescription of antivirals or antibiotics were recorded as documented in the medical record and laboratory computer system.

Statistical analysis

Demographic variables and clinical characteristics were compared using multiway contingency tables and computing Chi-square values. Fisher's exact test was used for variables with $n \leq 5$. Two-sided t-tests were used to compare numerical data. For all variables, influenza negative patients were

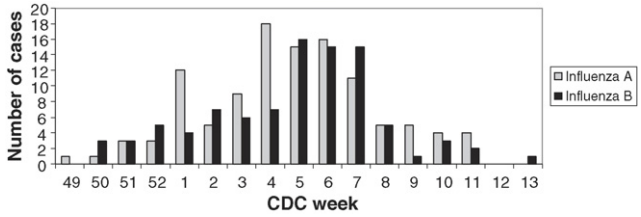

Figure 1 Influenza cases in Houston for the 2002—2003 season.

compared to influenza positive patients, and the influenza A group was compared to the influenza B group. All analyses were univariant, as this was a descriptive study. For all tests, $p < 0.05$ was considered significant. Incidence of influenza A and B was estimated based on the midyear age specific population of Harris County (Houston) in 2002—2003. Hospitalization rates were calculated based on the proportion of pediatric hospital beds at Texas Children's Hospital in relation to the total number of pediatric beds available in the county.

Results

Influenza peaked in the Houston area during January and February (CDC weeks 1—8) (Figure 1), similar to the 2002—2003 national data from the Centers for Disease Control and Prevention (CDC). Co-circulation of influenza A (54.6% of cases, more than two thirds A/H1N1) and influenza B (45.4% of cases, practically all Victoria B lineage) was observed throughout the epidemic.[17] There were 211 laboratory-confirmed cases of influenza at Texas Children's Hospital during the study period; 205 (97%) of the charts were available for review. The charts of 206 children with influenza-like illness, but negative influenza rapid tests and cultures, were also reviewed.

The majority of influenza cases (56%) were diagnosed by viral culture. The observed sensitivity of the Directigen Flu A/B™ rapid test for influenza A was 46.7% and for influenza B was 37.8%, or 45.8% overall. This was lower than the expected sensitivity (72—86%) for this test. Specificity was 97% as predicted.[18] Of note, this poorly sensitive test was subsequently removed from the market.

Influenza positive vs. influenza negative children

The study groups had a similar distribution of demographic characteristics such as age, gender, ethnicity, and insurance status (Table 1). Children with laboratory-confirmed influenza were more likely to be previously healthy while influenza negative children were more likely to have chronic

Table 1 Patient demographics for each group

	Influenza neg. no. (%)[a]	Influenza A/B no. (%)[a]	Influenza A no. (%)[a]	Influenza B no. (%)[a]
Total	$n = 206$	$n = 205$	$n = 112$	$n = 93$
Gender				
Male	117 (57)	103 (50)	61 (54)	42 (45)
Female	89 (43)	102 (50)	51 (46)	51 (55)
Age				
Average (years)	5.5	5.5	4.6	6.7[b]
<6 months	36 (17)	33 (16)	25 (22)	8 (9)
6—23 months	36 (17)	39 (19)	23 (21)	16 (17)
2—18 years	134 (65)	133 (65)	64 (57)	69 (74)
Ethnic origin				
White	79 (38)[c]	48 (23)	18 (16)	30 (32)[b]
Black	42 (20)	56 (27)	38 (34)	18 (19)
Hispanic	78 (38)	94 (46)	53 (47)	41 (44)
Other	7 (3)	7 (3)	3 (3)	4 (4)
Insurance				
Medicaid	80 (39)	83 (40)	49 (44)	34 (37)
Private	91 (44)	84 (41)	42 (38)	42 (45)
None/self	35 (17)	38 (19)	21 (19)	17 (18)
Health status				
Healthy	64 (31)	106 (52)[c]	59 (53)	47 (51)
Underlying conditions	142 (69)[c]	99 (48)	53 (47)	46 (49)
Exposures				
Patient in daycare	20/192 (10)	20/180 (11)	14/98 (14)	6/82 (7)
Patient in school	80/192 (42)	81/180 (45)	35/98 (36)	46/82 (56)[b]
Siblings at home	146/210 (70)	137/187 (73)	79/104 (76)	58/83 (70)
Known ill contacts	49/198 (25)	80/196 (41)[c]	46/108 (43)	34/88 (39)

[a] Due to rounding, percentages may not sum to 100.
[b] Statistically significant difference with $p < 0.05$.
[c] $p < 0.005$.

Table 2 Presence of underlying conditions in each study group

	Influenza neg. no. (%)	Any influenza no. (%)	Influenza A no. (%)	Influenza B no. (%)
Total	206	205	112	93
Patients with at least one:	142 (69)[a]	99 (48)	53 (47)	46 (49)
Prematurity	21 (10)	23 (11)	13 (12)	10 (11)
BPD	12 (6)	9 (4)	6 (5)	3 (3)
RAD	54 (26)	32 (16)	19 (17)	13 (14)
Other pulmonary disease	26 (13)[b]	12 (6)	2 (2)	10 (11)
Cardiovascular disease	21 (10)	14 (7)	10 (9)	4 (4)
Neuromuscular disease	22 (11)	11 (5)	3 (3)	8 (9)
Immunodeficiency	5 (2)	3 (1)	3 (3)	0 (0)
Malignancy	26 (13)[b]	9 (4)	3 (3)	6 (6)
Transplant recipient	19 (9)[a]	8 (4)	3 (3)	5 (5)
Immunosuppressed	31 (15)[b]	12 (6)	5 (4)	7 (8)

BPD, bronchopulmonary dysplasia; RAD, reactive airways disease.
[a] Statistically significant difference $p < 0.05$.
[b] $p < 0.005$.

medical conditions; 69% compared to only 48% for the influenza positive cases (OR 0.42, 95% CI 0.28—0.64, $p = 0.00003$). The distribution of the different medical conditions found in both groups was similar, with the exception of a greater frequency of pulmonary diseases other than asthma, and immunosuppressive conditions (including malignancy and organ transplantation) in the influenza negative group (Table 2). The children with negative influenza tests were diagnosed with an assortment of viral and bacterial infections, most commonly bacterial tracheitis or pneumonia (30%), parainfluenza virus (6.8%), and respiratory syncytial virus (4.4%).

At the time of initial evaluation, children with laboratory-confirmed influenza were significantly more likely to present with fever (OR 3.7, 95% CI 2.17—6.37, $p < 0.005$), rhinorrhea or congestion (OR 1.9, 95% CI 1.26—2.88, $p < 0.005$), or cough (OR 1.6, 95% CI 1.1—2.57, $p < 0.05$) when compared to influenza negative patients (Table 3). Children with respiratory diseases other than influenza presented more frequently with shortness of breath and difficulty breathing (OR 0.44; 95% CI 0.25—0.76, $p < 0.005$). When the occurrence of clinical symptoms in different age groups was analyzed, fever was significantly more common in children with laboratory-confirmed influenza at all ages, but particularly in infants <6 months of age (OR 6.8, 95% CI 1.9—25.3, $p < 0.005$). Older children with influenza were more likely to present with a cough (OR 3.3, 95% CI 1.86—5.8, $p < 0.005$), while decreased feeding was often reported in infants <6 months of age (OR 6.7, 95% CI 1.23—28.4, $p < 0.05$) (Table 4). Febrile seizures occurred in approximately 5% of children in both study groups, and no cases of encephalitis occurred in either patient population.

Table 3 Patient symptoms at the time of presentation for evaluation of influenza or influenza-like illness

	Influenza neg. no. (%) $n = 206$	Influenza A/B no. (%) $n = 205$	Influenza A no. (%) $n = 112$	Influenza B no. (%) $n = 93$
Days of illness, mean (range)	3.4 (0—30)	3.6 (0—60)	3.8 (0—60)	3.4 (0—21)
Fever	136 (66)	180 (88)[a]	95 (85)	85 (91)
Rhinorrhea/congestion	96 (47)	128 (62)[a]	67 (60)	61 (66)
Cough	118 (57)	142 (69)[b]	70 (63)	72 (77)
SOB/diff. breathing	51 (25)[a]	26 (13)	11 (10)	15 (16)
Vomiting/diarrhea	59 (29)	77 (38)	39 (35)	38 (41)
Headache	28 (14)	37 (18)	17 (15)	20 (22)
Sore throat	29 (14)	33 (16)	14 (13)	19 (20)
Myositis	24 (12)	25 (12)	8 (7)	17 (18)[b]
Stomach ache	14 (7)	7 (3)	2 (2)	5 (5)
Seizure	9 (4)	9 (4)	4 (4)	5 (5)
Chest pain	5 (2)	6 (3)	3 (3)	3 (3)
Decreased oral intake	15 (7)	25 (12)	15 (13)	10 (11)
Apnea	8 (4)	4 (2)	2 (2)	2 (2)
Cyanosis	10 (5)	8 (4)	4 (4)	4 (4)
Other	36 (17)	32 (16)	17 (15)	15 (16)

SOB, shortness of breath.
[a] $p < 0.005$.
[b] Statistically significant $p < 0.05$.

Table 4 Prevalence of clinical presentations by age, expressed as the percentage of patients in each group with these symptoms at the time of presentation

	Influenza negative (%)			Influenza positive (%)		
	<6 mo *n* = 36	6–23 mo *n* = 36	2–18 years *n* = 134	<6 mo *n* = 39	6–23 mo *n* = 33	2–18 years *n* = 133
Fever	49	51	74	88[a]	82[b]	89[a]
Rhinorrhea/congestion	73	63	54	94	69	61
Cough	73	60	52	82	62	78[a]
SOB/diff. breathing	32	34	19	15	26	10
Vomiting/diarrhea	22	20	31	33	38	45
Headache	0	0	21	0	0	28
Sore throat	0	0	22	0	3	24
Myalgia/myositis	0	0	18	0	0	20
Stomach ache	0	0	12	0	0	5
Seizures	3	0	5	0	5	5
Chest pain	0	0	4	0	0	5
Decreased oral intake	3	14	7	27[b]	13	8
Apnea	16	3	1	12	0	0
Cyanosis	14	3	3	15	5	1
Other	8	20	17	12	21	17

SOB, shortness of breath.
[a] $p < 0.005$.
[b] Statistically significant $p < 0.05$.

These symptoms were consistent with the severity of illness ranking, demonstrating that patients with influenza more often presented with febrile upper respiratory illness, while influenza negative patients had more lower respiratory tract disease (Table 5). Consequently, children with infections other than influenza more frequently required supplemental oxygen (OR 0.38, 95% CI 0.22–0.64, $p < 0.005$) and mechanical ventilation (OR 0.34, 95%CI 0.12–0.93, $p < 0.05$). Leukocytosis was also more common in the influenza negative group (Table 6). In addition, children in this group were more likely to be hospitalized than children with laboratory-confirmed influenza (61% vs. 37%, respectively, OR 0.37, 95% CI 0.25–0.57, $p < 0.001$).

Among children with laboratory-confirmed influenza, the highest rate of hospitalization was seen in infants less than one year of age, 8 per 10 000 population, Table 7). Hospitalization was required in 24.5% of healthy children and 53.5% of children with chronic conditions ($p < 0.001$) for influenza. In children negative for influenza, hospitalization occurred in 36% of healthy patients and 72.5% of children with chronic conditions ($p < 0.001$).

Antibiotic use was common and in similar frequency in both study groups, while antivirals were seldom used and were more likely to be prescribed in children with laboratory-confirmed influenza (7% vs. 1% of influenza negative patients, OR 2.7, 95% CI 0.71–9.2, NS). The data we present are suggestive of overuse of antibiotics as 43% of children with a documented influenza virus infection received antibiotics unnecessarily. Furthermore, 59% of patients in the influenza negative group received antibiotics. Only 12/79 (15.2%) of these influenza negative children receiving antibiotics were diagnosed with a bacterial illness by laboratory evaluation.

Table 5 Severity of illness by group, expressed as the percentage of patients within each group (ex. influenza negative) who had each severity score

	Influenza negative (%) *n* = 206	Influenza A/B (%) *n* = 205	Influenza A (%) *n* = 112	Influenza B (%) *n* = 93
URI[a]	41	64[b]	68	59
OM/sinusitis	5	3	1	5
LRI	30[c]	18	18	17
GI[d]	7	8	7	9
Other[e]	17[c]	7	5	10

URI, upper respiratory infection; OM, otitis media; LRI, lower respiratory infection; GI, gastrointestinal.
[a] Each patient was placed in only one group, corresponding to their highest severity score; for example if they had a URI and OM, they were placed in the OM group.
[b] $p < 0.005$.
[c] Statistically significant $p < 0.05$.
[d] GI symptoms only, no signs of URI, OM or LRI.
[e] Patients without any of the above symptoms. Some tests were sent as pre-operative or pre-transplant work-up, others for non-specific symptoms such as myalgias.

Table 6 Patient laboratory findings, hospitalizations, complications and therapies for each group

	Influenza neg. no. (%) $n = 206$	Influenza A/B no. (%) $n = 205$	Influenza A no. (%) $n = 112$	Influenza B no. (%) $n = 93$
Oxygen	59 (29)[a]	27 (13)	11 (10)	16 (17)
Non-invasive ventilation	2 (1)	1 (0.5)	0	1 (1)
Mechanical ventilation	17 (8)[b]	6 (3)	2 (2)	4 (4)
Bacterial infection	17 (8)	23 (11)	8 (7)	15 (16)
WBC ($\times 10^9$ cells/L)	12.1[a]	9	9.6	8.3
Leukopenia $<2.5 \times 10^9$ cells/L	12 (6)	6 (3)	1 (1)	5 (5)
Leukocytosis $>20 \times 10^9$ cells/L	21 (10)[a]	4 (2)	4 (4)	0
Platelets (average) $\times 10^9$ cells/L	353	289	324[a]	252
Thrombocytopenia $<50 \times 10^9$ cells/L	7 (3)	4 (2)	1 (1)	3 (3)
Thrombocytopenia $<100 \times 10^9$ cells/L	11 (5)	12 (6)	3 (3)	9 (10)[b]
Thrombocytosis $>500 \times 10^9$ cells/L	34 (17)	15 (7)	10 (9)	5 (5)
Death	0	1	0	1
Hospitalization	126 (61)[a]	76 (37)	37 (33)	39 (42)
Length of stay (LOS) (days)	9.1	6.2	4	8.4
Range of LOS (days)	1–85	1–36	1–12	1–36
Antibiotic therapy	122 (59)	88 (43)	46 (41)	42 (45)
Antiviral therapy	3 (1)	15 (7)[b]	10 (9)	5 (5)

[a] $p < 0.005$.
[b] Statistically significant $p < 0.05$.

Children being admitted were more likely to receive antibiotics. Of the children admitted with influenza, 85.7% (60/70) received antibiotics, and 50% (30/60) of these children were under two years of age. Of the influenza negative children who were admitted, 74.6% (47/63) received antibiotics; in this group, 40.4% (19/47) were under two years of age.

No deaths occurred in the influenza negative group during the visit or hospitalization in which the influenza tests were sent. One death occurred in a patient with influenza B (Table 6). This seven-month-old infant had multiple other medical problems including chronic lung disease, gastroesophageal reflux disease, and significant hypoxic injury at birth, which resulted in placement of a ventriculoperitoneal shunt for hydrocephalus and a gastrostomy tube. He initially presented with pneumonia and sepsis requiring mechanical ventilation, support for hypotension, and antibiotics. His respiratory cultures grew influenza B and *Pseudomonas* species.

The subgroups of influenza positive ($n = 106$) and negative patients ($n = 64$) without underlying conditions were also examined. There were trends toward more fever, rhinorrhea, and cough at presentation in the influenza positive group, but these differences were not statistically significant. Otitis media was more frequently diagnosed in the influenza negative group (7 vs. 3 patients, $p = 0.042$). There was no difference in the incidence of lower respiratory tract disease. No significant differences were seen in laboratory values, the occurrence of complications, or length of hospital stay (data not shown). Twenty-six of the 106 (25%) otherwise healthy patients with influenza were hospitalized, as were 23 of the 64 (36%) influenza negative patients ($p = 0.1$). Only six (5.7%) of the 106 patients with laboratory-confirmed influenza received antivirals (two influenza negative also received antivirals). However, 33% of the healthy patients with influenza and 42% of the healthy influenza negative group received antibiotics.

Table 7 Hospitalization rates for influenza per 10 000 population

Age (years)	Influenza A/B	Influenza A	Influenza B
<1	8	5.3	2.8
1–4	1.8	1.2	0.6
5–8	1.6	0.6	1
10–14	1	0.2	0.9[a]
15–19	0.2	0.2	0.1
Total	0.7	0.4	0.4

[a] Statistically significant $p < 0.05$.

Influenza A vs. influenza B

Comparing cases of influenza A to influenza B, we noted that children with influenza B were on average two years older, and were more likely to be in school (Table 1). At the time of presentation, symptoms were similar in both groups except for an increased incidence of myositis or myalgia in older patients with influenza B (18% vs. 7%, OR 2.9, 95% CI 1.1–7.8, $p = 0.02$) (Table 3). We found no difference in the severity of illness between the influenza subtypes (Table 5).

Hospitalization was necessary in 33% of cases of influenza A and 42% of cases of influenza B (Table 7). The only laboratory differences between these two groups, was an elevated platelet count in the influenza A patients compared to thrombocytopenia in those with influenza B (Table 6).

Influenza immunization status

Immunization status was documented in 198 of the 411 (48%) study patients. Overall, only 23/198 (11.6%) children had received influenza vaccine. Twenty-three of 149 (15.4%) children with chronic high-risk conditions had been immunized. No healthy children of any age or mothers of infants

born during the influenza season reported receipt of influenza vaccine. Only 4/23 patients who received the influenza vaccine developed influenza, giving an estimated vaccine efficacy of 82.6%. All had underlying chronic diseases.

Discussion

The 2002–2003 influenza season in Houston, TX was characterized by an equal prevalence of influenza A and B viruses. Influenza B Victoria lineage had not circulated in the area for 12 years. The combination of these two factors made this an ideal season for comparing the clinical manifestations of these two viruses in children.

Texas Children's Hospital is a large referral center caring for patients with a variety of acute and chronic medical conditions. The latter tend to seek medical care more frequently than healthy children, use more services, and have more laboratory tests obtained. This probably accounts for the high number of children with underlying conditions in our study groups. Nevertheless, we observed that children with laboratory-confirmed influenza were significantly more likely to be previously healthy and seek medical attention exclusively for symptoms associated with influenza. This finding supports the concerns on the impact of influenza in otherwise healthy children.[6,11] The majority (65%) of children with laboratory-confirmed influenza were over two years of age and were more likely to report an exposure to an ill contact, usually at school. This is consistent with previous descriptions of high attack and transmission rates in school-aged children, and this season it concurred with the circulation of a strain of influenza B new to this age group. The variety of etiologic agents identified in the influenza negative group represented the spectrum of causes of influenza-like illnesses seen during the influenza season.

Children with laboratory-confirmed influenza were significantly more likely to present with symptoms that are nonspecific and limited to the upper airway. However, complications such as apnea, pneumonia, and secondary bacterial infections still occurred in children with laboratory-confirmed influenza, especially if under six months of age. Young infants are more likely to present with fever alone, or non-respiratory symptoms, such as decreased oral intake, vomiting, or diarrhea. Influenza-positive and influenza-negative children had a similar incidence of seizures, musculoskeletal, and gastrointestinal symptoms. The occurrence of febrile seizures in approximately 5% of our patients with influenza is consistent with previous reports.[16] Rare extrapulmonary complications of influenza such as encephalitis were not observed, likely due to our sample size, since encephalitis associated with influenza A was reported during this season.[19] Total hospitalization rates are probably underestimated in our study since diagnosis depended on respiratory culture without serology. Importantly, children with influenza who are otherwise healthy, present with symptoms that are indistinguishable from symptoms caused by other respiratory viruses. Influenza virus infection was more likely to result in emergency room and acute care visits in previously healthy children.[1,16]

Of note this season was the poor sensitivity of the rapid antigen detection test noted early in the epidemic. This was attributed to the specific test used, rather than to a laboratory error, as other laboratories had a similar experience.[20] The lack of a rapid diagnosis makes it difficult for clinicians to begin early antiviral therapy. In our study only 15 (7%) patients with influenza received antivirals. Antiviral use is influenced by the confirmation of influenza by rapid tests.[21] Almost 50% of the patients in both groups were given antibiotics, even though only 8–15% of them had a bacterial infection. This antibiotic prescription rate may be higher than normal due to the delay in diagnosis,[22] however, increased antibiotic prescribing during the winter months is not uncommon.[1,10]

The American Academy of Pediatrics (AAP) and the CDC's Advisory Committee on Immunization Practices current recommendations are that children six months of age or older receive influenza vaccine if they have chronic medical conditions. In 2002, the AAP stated that influenza vaccine should also be administered to healthy children 6–23 months of age due to the increased morbidity and hospitalization rates in this age group.[2,23] It is also recommended that household contacts of patients with underlying conditions or children 0–23 months of age, and pregnant women in their second and third trimesters receive vaccination prior to the start of the influenza season. No mothers of infants less than six months of age, or healthy children in our study received influenza vaccination. Only 15% of the children with high-risk conditions were vaccinated. This rate increased moderately from the <5% immunization rate reported during our 1997–1998 season,[24] but there is still a strong need for education of healthcare providers, and a better way to track the vaccine status of high-risk patients. The estimated vaccine efficacy of 82.6% is consistent with an antigenic match between the circulating and the vaccine strains.[25] During the 2002–2003 winter season influenza A (H1N1), A (H3N2), and influenza B Victoria lineage circulated. According to the CDC, of the influenza A strains, 85–100% of those typed were similar to the vaccine strains, and 100% of the influenza B strains tested were similar to the vaccine strains.[19]

In summary, most children with laboratory-confirmed influenza seeking medical attention were previously healthy. This is probably because of the high fever associated with influenza infection, particularly in young infants. We found no consistent clinical markers to distinguish influenza A or B from each other or other winter viral infections. The recirculation of the Victoria lineage of influenza B did not appear to increase the morbidity or hospitalization rate in children considered to be immunologically naïve, and the age group affected with influenza B tended to be older school-aged children. Education and improvement in influenza vaccination is still needed and should be prioritized in general pediatrics, subspecialty pediatrics, and obstetrics.

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