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# Prospective Evaluation of the Risk of Serious Bacterial Infection in Children Who Present to the Emergency Department With Hyperpyrexia (Temperature of 106°F or Higher)

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## ABSTRACT

**BACKGROUND.** Previous studies of children with temperatures  $\geq 106^\circ\text{F}$  (hyperpyrexia) disagree as to whether hyperpyrexia confers a high risk of serious bacterial infection.

**OBJECTIVES.** The purpose of this study was to determine (1) the risk of serious bacterial infection in children with hyperpyrexia and (2) whether clinical presentation can identify hyperpyrexia patients at risk for serious bacterial infection.

**METHODS.** Data were collected prospectively on all children  $< 18$  years of age presenting to a pediatric emergency department during a 2-year period with rectal temperatures of  $\geq 106^\circ\text{F}$ . History, physical examination, complete blood cell counts, blood cultures, and nasopharyngeal viral cultures were obtained on all of the patients.

**RESULTS.** Of 130 828 visits, 103 children had hyperpyrexia (1 per 1270 patient visits). Of the 103 subjects, 20 had serious bacterial infection, and 22 had laboratory-proven viral illness (including 1 subject with bacterial/viral coinfection). The presence of a chronic underlying illness was associated with an increased risk of serious bacterial infection. The presence of rhinorrhea or any viral symptom was associated with a decreased risk of serious bacterial infection, although diarrhea itself was associated with an increased risk of serious bacterial infection. Age, maximum temperature, and total white blood cell count were not predictive of either bacterial or viral illness.

**CONCLUSIONS.** Children with hyperpyrexia are at equally high risk for serious bacterial infection and for viral illness. Bacterial and viral coinfection also occurs. No aspect of the clinical presentation reliably distinguishes between bacterial and viral illness. We recommend consideration of antibiotic treatment for all children presenting to the emergency department with hyperpyrexia without confirmed viral illness.

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### Key Words

hyperpyrexia, emergency department, pediatric

### Abbreviations

ED—emergency department  
SBI—serious bacterial infection  
RSV—respiratory syncytial virus  
UTI—urinary tract infection  
CXR—chest radiograph  
WBC—white blood cell  
CSF—cerebrospinal fluid  
CI—confidence interval  
OR—odds ratio  
ANC—absolute neutrophil count  
IQR—interquartile range

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**H**YPERPYREXIA, DEFINED AS a rectal temperature  $\geq 106^{\circ}\text{F}$  ( $41.1^{\circ}\text{C}$ ), is considered a medical emergency and typically results in referral for emergency care. Children's higher metabolic rate and decreased thermoregulatory control, among other factors, put them at higher risk for heat stress than adults.<sup>1</sup> Hyperpyrexia is the presenting diagnosis in  $\sim 1$  in 2000 children who present to a pediatric emergency department (ED).<sup>2,3</sup> Common causes of hyperpyrexia in children include bacterial infections, viral infections, neuroleptic malignant syndrome, intoxication, and heat stroke.<sup>4</sup> As the evaluation and management of these etiologies varies considerably, identifying signs or symptoms that could guide subsequent workup would be very useful to pediatric emergency medicine practitioners. Furthermore, whether or not hyperpyrexia itself confers a high risk for serious bacterial infection (SBI) is a controversial issue.

Relatively few studies have addressed hyperpyrexia in children. Four studies of children with temperatures  $\geq 41.1^{\circ}\text{C}$  were performed before 1990. The largest of these was a retrospective analysis by McCarthy and Donlan<sup>5</sup> of 100 children seen in a pediatric ED between 1966 and 1974 with a temperature  $>41.1^{\circ}\text{C}$ . The comparison group was children seen in the ED with a temperature between  $40.5$  and  $41.0^{\circ}\text{C}$ . The presence of hyperpyrexia conferred a significantly greater risk of bacterial meningitis (19% in the hyperpyrexia group versus 8% in the comparison group). This finding of an association between hyperpyrexia and SBI was supported by a small prospective study of 15 children<sup>3</sup> but refuted by a second small prospective study in 19 children<sup>2</sup> and by a retrospective case-control study.<sup>6</sup> More recently, a retrospective analysis of infants  $<3$  months of age found that one third of infants with a temperature  $\geq 40.0^{\circ}\text{C}$  had an SBI.<sup>7</sup> However, this finding cannot necessarily be applied to children  $>3$  months of age, and the cutoff for hyperpyrexia was also lower than that in previous studies.

Overall, the findings from hyperpyrexia studies from the past may not be germane to current ED practices. The introduction of the *Haemophilus influenzae* type b conjugate vaccine in 1987 has led to a marked decrease in the incidence of meningitis caused by *H influenzae* type b.<sup>8</sup> In the McCarthy and Donlan<sup>5</sup> study of hyperpyrexia, 7 of the 10 cases of bacterial meningitis were caused by *H influenzae* type b, so their findings may no longer be relevant. Furthermore, viral studies were not performed in any of these hyperpyrexia studies, and rapid viral testing is now a valuable tool in the ED evaluation of febrile children. The purpose of our study was to evaluate the incidence of SBI in children presenting to the ED with hyperpyrexia and to determine whether any aspects of their presentation were predictive of the risk of SBI.

## METHODS

### Design

The study is a cross-sectional observational study.

### Setting

The Texas Children's Hospital ED is part of a tertiary care pediatric hospital in Houston, TX, with  $\sim 80\,000$  visits annually. At the time of this study, this ED was staffed by attending physicians 24 hours per day.

### Selection of Participants

The standard ED protocol is to measure all children's temperatures at triage. From September 24, 1998, to September 24, 2000, children who had an oral, axillary, or ear temperature  $>104^{\circ}\text{F}$  ( $40^{\circ}\text{C}$ ) had a rectal temperature obtained. All of the children with a rectal temperature  $\geq 106^{\circ}\text{F}$  ( $41.1^{\circ}\text{C}$ ) were enrolled in the study. Enrolled subjects had a complete history and physical examination performed by a pediatric ED fellow or attending. There were no exclusion criteria. Subjects received the standard of care for evaluation and management of hyperpyrexia in this institution. This study was approved by the Baylor College of Medicine Institutional Review Board.

### Clinical and Laboratory Assessment

Each subject was assessed for the following viral symptoms by the pediatric ED fellow or attending: rhinorrhea, vomiting, diarrhea, sweating, and conjunctival injection. Per study protocol, initial laboratory evaluation for all of the children included a complete blood cell count with differential, blood culture, and viral cultures of the nasopharynx. The viral cultures were obtained via nasopharyngeal washes by trained respiratory therapists. Nasopharyngeal samples were tested by cell cultures for all cultivatable viruses, including respiratory syncytial virus (RSV), influenza A and B, parainfluenza viruses types 1 to 4, adenovirus, picornaviruses, rhinoviruses, enteroviruses, herpes simplex viruses types 1 and 2, varicella zoster virus, and cytomegalovirus. Urine for analysis and culture was obtained in all of the patients  $<2$  years of age without a source for their fever and from any patient with a history of dysuria, urinary frequency, previous urinary tract infection (UTI), or renal abnormalities. Lumbar puncture was performed in children with clinical suspicion for meningitis. Chest radiograph (CXR) was obtained in children with respiratory complaints, clinical suspicion of pneumonia by examination, or in any child  $<3$  years of age with a white blood cell (WBC) count of  $>20 \times 10^3$  cells per  $\text{mm}^3$  and no other source of infection. Stool bacterial and viral cultures were sent for children with significant diarrhea. Stool viral cultures will detect adenovirus, enterovirus, and cytomegalovirus. The above studies were specified by study protocol and were considered standard of care.

Other studies were performed at the discretion of the attending physician, including cultures of abscesses or wounds and rapid testing for *Streptococcus pyogenes*, RSV, or influenza A. Decisions concerning treatment and disposition were made by the attending physician.

### Definitions

Any chronic condition resulting in impaired function of any organ system was classified as an underlying condition, with the exception of reactive airways disease. The presence of foreign bodies, such as central intravascular catheters, ventriculoperitoneal shunts, and renal stents, was also classified as an underlying condition, as was a previous history of UTI, because the history of UTI could be a marker for renal structural abnormality.

The following organisms in blood cultures were considered to be contaminants, unless regarded as significant by the treating physician: coagulase-negative staphylococci,  $\alpha$ -hemolytic streptococci, or diphtheroids. UTIs were defined as the growth of a single pathogen of  $\geq 10^4$  colony-forming units per mL or  $\geq 10^5$  colony-forming units per mL on a clean catch specimen. Pneumonia was diagnosed if the attending radiologist read a focal parenchymal density on CXR (including the phrase bronchopneumonia) on routine dictation. The radiologists were blinded to the physician's interpretation and treatment plans. SBI was defined as the growth of a clinically significant bacterial pathogen from blood, urine, stool, cerebrospinal fluid (CSF), or any normally sterile body site. A viral illness was defined as the recovery of virus from nasopharyngeal or stool cultures or by a positive rapid test for viral antigens.

### Statistical Analysis

Statistical analyses were performed using SPSS for Windows (SPSS Inc, Chicago, IL). Overall frequencies of subject ages, gender, ethnicity, and viral symptoms were calculated with 95% confidence intervals (CIs). Age was dichotomized into 3 to 35 months and  $\geq 36$  months. Overall frequencies of final diagnoses were also calculated with 95% CIs. The types of bacterial and viral pathogens were quantified. Subject treatment and disposition were also described.

Odds ratios (ORs) and 95% CIs were used to explore the association among age, duration of fever, underlying medical condition, WBC count, absolute neutrophil count (ANC), and viral symptoms with bacterial or viral illness. WBC count was categorized as  $< 15 \times 10^3$  and  $\geq 15 \times 10^3$  cells per  $\text{mm}^3$ . ANC was categorized as  $< 10 \times 10^3$  and  $\geq 10 \times 10^3$  cells per  $\text{mm}^3$ . Receiver operating characteristic curves were created to determine how well WBC count, ANC, and absolute band count would predict the presence of bacterial or viral illness.

## RESULTS

### Study Population

During the 2-year study period, there were 130 828 visits to the ED, and 103 children had hyperpyrexia, defined as a rectal temperature  $\geq 106^\circ\text{F}$  ( $41.1^\circ\text{C}$ ; 1 per 1270 patient visits). All 103 of the children with hyperpyrexia were enrolled in the study. Subjects' ages ranged from 3 months to 16.9 years with a median of 17 months (interquartile range [IQR]: 11–25 months). The distributions of subject age, gender, and ethnicity are presented in Table 1. No child under the age of 3 months seen in the ED during the 2-year period of the study had a temperature  $\geq 41.1^\circ\text{C}$  ( $106^\circ\text{F}$ ). The median rectal temperature recorded in the ED was  $106.2^\circ\text{F}$  (IQR:  $106.1$ – $106.5$ ), with a maximum of  $108.9^\circ\text{F}$ . For the 103 subjects, the median WBC count was  $15.0 \times 10^3$  cells per  $\text{mm}^3$  (IQR:  $9.6$ – $22.0$ ). Table 2 presents the frequency of studies performed on study subjects, as well as the rates of positive study results.

### Diagnoses

The final diagnoses are presented in Table 3, and culture results are presented in Table 4. Overall, of the 103 subjects, 20 had a culture-proven SBI (18.4%), including 1 subject who had both a bacterial and a viral infection. Eleven of the subjects had bacteremia, including 2 who were bacteremic secondary to UTI and 2 with bacteremia secondary to infection of an indwelling central venous catheter. One of the subjects with bacteremia secondary to an intravascular catheter infection had 4 different species of Gram-negative organisms recovered

TABLE 1 Characteristics of 103 Subjects With Hyperpyrexia

Characteristic	Frequency (N = 103), n (%)	95% CI
Age, mo		
3–35	87 (84.5)	77.5–91.5
$\geq 36$	16 (15.5)	8.5–22.5
Gender		
Male	57 (55.3)	45.7–64.9
Female	46 (44.7)	35.1–54.3
Ethnicity		
Black	49 (47.6)	37.9–57.2
Hispanic	38 (36.9)	27.6–46.2
White	12 (11.7)	5.5–17.9
Asian	4 (3.9)	0.2–7.6
Symptoms		
Rhinorrhea	62 (60.2)	50.7–69.7
Vomiting	36 (35.0)	25.8–44.2
Diarrhea	17 (16.5)	9.3–23.7
Injected conjunctivae	10 (9.7)	4.0–15.4
Any viral symptom	80 (77.7)	69.7–85.7
Duration of fever, h		
$< 24$	33 (32.0)	23.0–41.0
24 to $< 48$	34 (33.0)	24.0–42.0
$> 48$	36 (35.0)	25.8–44.2
Preexisting condition	19 (18.4)	10.9–25.9

**TABLE 2 Studies Completed for 103 Subjects With Hyperpyrexia**

Study	Completed Frequency (N = 103), n (%)	Positive Frequency, n (%)
Bacterial culture		
Blood	100 (97.1)	11 (11.0)
Urine	80 (77.7)	8 (10.0)
CSF	14 (13.6)	0 (0.0)
Stool	13 (12.6)	1 (7.7)
Viral culture		
Nasopharyngeal	96 (93.2)	17 (17.7)
Stool	20 (19.4)	4 (20.0)
Rapid viral tests		
RSV	20 (19.4)	3 (15.0)
Influenza	17 (16.5)	2 (11.8)
CXR	52 (50.5)	18 (34.6)

**TABLE 3 Final Diagnoses for 103 Subjects With Hyperpyrexia**

Diagnosis	Frequency (N = 103), n (%)	95% CI
Febrile illness without positive cultures	60 (58.3)	48.8–67.8
Viral illness with positive culture	21 (20.4)	12.6–28.2
Bacterial illness with positive culture	19 (18.4)	10.9–25.9
Positive viral and bacterial cultures	1 (1.0)	0.0–2.9
Neuroleptic malignant syndrome	1 (1.0)	0.0–2.9
Systemic lupus erythematosus	1 (1.0)	0.0–2.9

from blood cultures: *Enterobacter cloacae*, *Escherichia coli*, *Citrobacter freundii*, and *Stenotrophomonas maltophilia*. Eight subjects had a UTI, including a 3-month-old boy who grew *E coli* from urine and blood. This child also had meningitis by CSF parameters (WBC count of 269 cells per mm<sup>3</sup>; 95% neutrophils) and was treated as such, but his CSF was collected after >12 hours on antibiotics and showed no growth. One subject, a 4-year-old boy with muscular dystrophy, presented with both neuroleptic malignant syndrome and apparent septic shock. His temperature reached 108.9°F, and he expired during subsequent hospitalization despite aggressive management. A tracheal aspirate collected in the ED grew *Pseudomonas*. Because the same organism was recovered from autopsy blood cultures, the *Pseudomonas* was regarded as the cause of sepsis. The subject who had both positive bacterial and viral cultures was a 25-month-old female with sickle cell anemia who presented to the ED with a septic appearance. Her nasopharyngeal viral swab tested positive for RSV, and her blood also grew an  $\alpha$ -hemolytic streptococcus, which was judged to be a true bacteremia by the infectious diseases service during the patient's subsequent hospitalization. Other etiologies for SBI included dysentery caused by *Shigella flexneri* and an epidural abscess, which grew *Peptostreptococcus magnus*.

In terms of establishing the diagnosis of SBI in the ED, 2 of the 20 subjects with culture-proven SBI had a CXR compatible with lobar pneumonia; both of these subjects also grew *Streptococcus pneumoniae* from the blood. The 2

**TABLE 4 Culture Results for 103 Subjects With Hyperpyrexia**

Culture Source	Organism	Frequency
Blood	<i>S pneumoniae</i>	4
	<i>E coli</i> <sup>a</sup>	3
	<i>E cloacae</i>	1
	<i>Alpha streptococcus</i> <sup>b</sup>	1
	<i>Klebsiella pneumoniae</i> <sup>c</sup>	1
	Multiple GNR <sup>c</sup>	1
Epidural abscess	<i>P magnus</i>	1
Tracheal aspirate	<i>Pseudomonas aeruginosa</i>	1
Urine	<i>E coli</i> <sup>a</sup>	6
	<i>E cloacae</i>	1
	<i>Enterococcus</i> species	1
Stool bacterial	<i>S flexneri</i>	1
Stool viral culture	Enterovirus	2
	Adenovirus <sup>d</sup>	2
Nasopharynx	Adenovirus <sup>d</sup>	7
Viral cultures	Influenza A <sup>e</sup>	4
	RSV	3
	Parainfluenza 3	1
	Picornavirus	1
	Cytomegalovirus	1
Nasopharynx		
Rapid viral tests	RSV <sup>b,d</sup>	3
	Influenza A <sup>e</sup>	2

<sup>a</sup> Two subjects with *E coli* UTI also grew *E coli* from the blood, including 1 with meningitis by CSF parameters.

<sup>b</sup> One subject had a positive RSV rapid test and also grew  $\alpha$  streptococcus from blood culture.

<sup>c</sup> Source was judged to be an infected central venous catheter.

<sup>d</sup> Two subjects grew adenovirus from both stool and nasopharyngeal viral cultures. One subject with adenovirus also had a positive RSV rapid viral test.

<sup>e</sup> One subject grew influenza A from the nasopharyngeal culture and had a positive rapid test for influenza. There was no other overlap between rapid viral test results and cultures.

other subjects with *S pneumoniae* bacteremia had negative CXR results. None of the 20 children with positive bacterial cultures were thought to have otitis media on physical examination.

The number of subjects with culture- or rapid test-proven viral illness was 22 (21.4%) of 103 including 7 with adenovirus, 1 with picornavirus, 2 with enterovirus, 6 with RSV, 5 with influenza A, 1 with cytomegalovirus, and 1 with parainfluenza 3. Of the 6 subjects with RSV, 1 grew adenovirus from a nasopharyngeal wash, and another subject with RSV also had  $\alpha$ -hemolytic streptococcal bacteremia. The 2 subjects who grew adenovirus from stool viral cultures also grew adenovirus from nasopharyngeal cultures, whereas the 2 with enterovirus in the stool had negative nasopharyngeal viral cultures. Three of the 22 subjects with proven viral illness had a lobar infiltrate on CXR. These subjects' diagnoses were coinfection with adenovirus and RSV, adenovirus alone, and influenza A. Only 1 child in the viral illness group, also with influenza A, was diagnosed with otitis media by physical examination.

Of the remaining 62 subjects with hyperpyrexia, 60 were diagnosed with a febrile illness with negative cultures. One 7-year-old boy developed neuroleptic malignant syndrome in response to malfunction of his ventriculoperitoneal shunt. Another subject, a 16-year-old

girl with renal stents and recurrent pyelonephritis, was ultimately diagnosed with new onset of systemic lupus erythematosus during hospitalization. Of the 60 with negative cultures and no other diagnosis to account for their fever, 13 had a CXR with a lobar infiltrate compatible with pneumonia, and 11 were diagnosed with otitis media by physical examination (including 2 with both pneumonia and otitis media). Interestingly, although daily temperatures in Houston exceed 90°F for several months of the year, none of the children with hyperpyrexia in the ED had heat-related illness, nor were any children with hyperpyrexia diagnosed with hyperthermia secondary to ingestion.

### Outcomes

Of the 103 subjects, 28 (27.2%) were admitted to the hospital, and 75 (72.8%) were discharged from the hospital. One subject with muscular dystrophy died of neuroleptic malignant syndrome and sepsis, as described above. Of those discharged from the hospital, 35 (46.7%) were given intramuscular ceftriaxone, and 1 (1.3%) was given intravenous cefotaxime before discharge. Of the 39 subjects who did not receive intramuscular or intravenous antibiotics in the ED, 10 (25.6%) went home with a prescription for antibiotics. Of the 8 subjects with otitis media who were discharged from the hospital from the ED, all were prescribed antibiotics. Of the 29 who neither received antibiotics nor were prescribed antibiotics in the ED, 3 had an SBI. One of the subjects with an untreated SBI was a 16-month-old girl who presented with a febrile seizure after 3 days of fever. Her blood culture grew *E coli*. Another subject with untreated SBI was a 14-month-old girl with polycystic kidney disease who presented with fever and diarrhea. She subsequently grew *E cloacae* from blood cultures. Also, a 10-month-old girl grew *E cloacae* from urine culture. The WBC counts of these subjects, 11.9, 6.8, and  $10.9 \times 10^3$  cells per  $\text{mm}^3$ , respectively, were not markedly elevated and, indeed, were lower than the median WBC count of subjects with hyperpyrexia ( $15 \times 10^3$  cells per  $\text{mm}^3$ ). These relatively normal WBC counts may have misled the treating physician into suspecting a viral etiology. In all of the cases of hyperpyrexia, subjects were scheduled to receive follow-up with their primary care physician on the following day, as per ED practice.

### Predictors of SBI

Table 5 presents the ORs for the associations between possible predictive variables and confirmed bacterial illnesses. There was a trend toward increased risk of bacterial illness in children  $\geq 36$  months old. As expected, the presence of an underlying medical condition was associated with an increased risk of bacterial illness. The incidence of SBI in children with underlying illness was 7 (36.8%) of 19, whereas the incidence of SBI in children without underlying illness was 13 (15.5%) of 84.

**TABLE 5 Predictors of Bacterial Illness for 103 Subjects With Hyperpyrexia**

Variable	Bacterial (N = 20)	
	Frequency, n (%)	OR (95% CI)
Age, mo		
3–35	14 (70)	Ref
$\geq 36$	6 (30)	3.13 (0.98–10.01)
Preexisting condition	7 (35)	3.19 (1.06–9.61)
Duration of fever, h		
<24	8 (40)	Ref
24 to <48	3 (15)	0.30 (0.07–1.26)
>48	9 (45)	1.04 (0.35–3.12)
Viral symptoms		
Rhinorrhea	7 (35)	0.27 (0.09–0.76)
Vomiting	6 (30)	0.76 (0.26–2.18)
Diarrhea	7 (35)	3.93 (1.27–12.19)
Injected conjunctivae	1 (5)	0.43 (0.05–3.63)
Any viral symptom	12 (60)	0.33 (0.12–0.95)
WBC count, $\times 10^3$ cells per $\text{mm}^3$		
<15	11 (55)	Ref
$\geq 15$	9 (45)	0.78 (0.29–2.08)
ANC, $\times 10^3$ cells per $\text{mm}^3$		
<10	9 (45)	Ref
$\geq 10$	11 (55)	1.11 (0.41–2.96)

Ref indicates reference range.

The presence of rhinorrhea or any viral symptom was associated with a decreased risk of bacterial illness. However, the presence of diarrhea was associated with an increased risk of bacterial illness. There were no significant predictors of viral illness, although the presence of any viral symptom approached significance (OR: 2.08; 95% CI: 0.56–7.76). Neither WBC count nor ANC was predictive of bacterial or viral illness, either by ORs or by receiver operating characteristic curves. Likewise, the absolute band count was not predictive of either bacterial or viral illness. The median WBC count was slightly higher for viral illness ( $15.3 \times 10^3$  cells per  $\text{mm}^3$ ; IQR: 10.1–19.1) than for bacterial illness ( $14.4 \times 10^3$  cells per  $\text{mm}^3$ ; IQR: 10.5–24.2), although this difference was not statistically significant. Of the 5 subjects with a positive rapid viral test (3 RSV and 2 influenza), 1 had concurrent bacteremia, 2 had a CXR consistent with lobar pneumonia, 4 were ill enough to warrant hospitalization, and all but 1 were treated with antibiotics.

### DISCUSSION

Based on these results, children presenting to ED with hyperpyrexia are at high risk for SBI. They are also at equally high risk for a viral illness, and coexistence of both bacterial and viral illness was observed in 1 case (1%). Other than the presence of a preexisting medical condition, such as an anatomic abnormality predisposing to infection, no factor was predictive of SBI rather than viral infection. Specifically, the WBC count was not useful to distinguish between bacterial and viral infection, and a near normal WBC count may have led to failure to

prescribe antibiotics to 3 children with SBI. Similarly, viral symptoms were not a reliable guide to etiology of fever, because viral symptoms overall were associated with a decreased risk of SBI, but diarrhea was associated with an increased risk. The association of diarrhea with bacterial illness was surprising. One possible explanation is that diarrhea may be more common as a presenting symptom of UTI than is widely appreciated.<sup>9</sup> Our results suggest that all children who have a rectal temperature of  $\geq 106^{\circ}\text{F}$  and no proven viral etiology should be considered for antibiotic therapy, especially those with underlying chronic illnesses.

The increased sensitivity and availability of rapid viral testing has led to greater awareness of bacterial and viral coinfection. Based on our results, a positive rapid viral test may not be sufficient evidence to warrant nontreatment with antibiotics, given that 1 (1%) of 103 subjects had a bacterial and viral coinfection. However, this subject's symptoms at presentation were severe enough to require hospitalization. A study performed in the same ED of febrile children ages 0 to 36 months found that the prevalence of SBI was lower in those with a positive rapid antigen test for influenza A than in those without confirmed influenza.<sup>10</sup> However, the rate of culture-positive bacterial illness in that study was still 3 (1.8%) of 163 children with influenza. Two recent studies in hospitalized children with community-acquired pneumonia found a 23% to 35% prevalence of bacterial and viral coinfection in children with a lobar infiltrate on CXR.<sup>11,12</sup> Clinical signs and symptoms, including radiologic findings, were not a reliable guide to either viral or bacterial etiology. In our study, of the 18 children with a lobar infiltrate on CXR, 3 (16.7%) were in children with proven viral illness. Although these children had negative blood cultures, they could have had undetected bacterial pneumonia superimposed on a viral illness. The immune response to respiratory virus infections may indeed predispose to subsequent viral infections.<sup>13</sup> Whether clinically stable patients with hyperpyrexia and a positive rapid viral test should routinely receive antibiotics is unclear, but it certainly seems prudent to continue to treat all children with a lobar infiltrate on CXR with antibiotics.

Our findings should be interpreted with awareness that the sample size was limited to the 103 children who presented with hyperpyrexia during the 2-year study period. The sample size may have led us to underestimate the strength of the association of age  $\geq 36$  months with SBI. However, our sample size is unlikely to have affected the predictive value of WBC count for bacterial infection, because the median WBC count was actually higher with viral than with bacterial infection. To our knowledge, our study is the largest prospective study of hyperpyrexia in children.

Another factor that affects the applicability of our study results is that the time period of the study was

before the widespread use of the conjugate pneumococcal vaccine in children. However, in the 20 children with confirmed SBI, *S pneumoniae* was the causative agent in only 4 (20%) of the cases. Assuming 100% vaccine effectiveness, penetration, and strain coverage, 16 (15.5%) of the 103 children with hyperpyrexia would still have had an SBI despite use of the conjugate pneumococcal vaccine. We did not collect data on immunization status for the vaccines available at the time of data collection, because parents' recall in the ED may be inaccurate. As expected, no child in this study had a documented infection with *H influenzae*. Other than *S pneumoniae*, the causative agents of SBI in our subjects would not have been preventable by vaccination.

The majority of febrile children in this study (60 of 103 [58%]) did not have an identified etiology for their fever. We suspect that viruses may have been responsible for many of the nonspecific febrile illnesses. Human herpesvirus 6 is a well-documented cause of febrile illness in the pediatric population,<sup>14</sup> and human herpesvirus 6 testing was not performed during this study. Many viruses are not identifiable, and viral testing is  $<100\%$  sensitive. Illnesses that were yet evolving into an identifiable pattern, such as a characteristic viral exanthem, would have been classified as a nonspecific febrile illness. However, given that bacteremia can be intermittent and that our study captured data from a single ED visit, some of the subjects without an identified etiology of fever could, likewise, have had an SBI.

One interesting observation in our study is that no child with hyperpyrexia was under the age of 3 months. Only 1 child with hyperpyrexia was 3 months old, and this infant was found to have meningitis, as well as *E coli* UTI and bacteremia. Possibly infants this young cannot mount a fever as high as  $106^{\circ}\text{F}$ ; 1 study found that the metabolic rate of neonates decreases in response to infection.<sup>15</sup> Another interesting observation is that no child arrived in the ED with hyperpyrexia secondary to heat-related illness. We suspect that aggressive prehospital treatment to lower the body temperature of children with heat illness accounted for the absence of any cases of heat-induced hyperpyrexia among all of the children seen in a busy ED in Houston over a 2-year period.

## CONCLUSIONS

Our study is the largest prospective study of hyperpyrexia in the post-*H influenzae* type b vaccination era. We conclude that hyperpyrexia is a medical emergency that carries a high risk of SBI. These findings should hold true despite the subsequent introduction of the conjugate pneumococcal vaccine. We advise treatment with antibiotics for all children with hyperpyrexia who do not have a confirmed viral illness and for all children with hyperpyrexia and a confirmed viral illness who are ill enough to require hospitalization. Hyperpyrexia warrants medical evaluation for SBI.

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## LITIGOSIS

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*Wall Street Journal*. April 26, 2006

Noted by JFL, MD

**Prospective Evaluation of the Risk of Serious Bacterial Infection in Children Who Present to the Emergency Department With Hyperpyrexia (Temperature of 106°F or Higher)**

Barbara W. Trautner, A. Chantal Caviness, Gary R. Gerlacher, Gail Demmler and Charles G. Macias

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