

Empyema Hospitalizations Increased in US Children Despite Pneumococcal Conjugate Vaccine



WHAT'S KNOWN ON THIS SUBJECT: *Streptococcus pneumoniae* is the most common cause of community-acquired pneumonia and empyema. Although the PCV7 has decreased the incidence of invasive pneumococcal disease, the vaccine's effectiveness in reducing empyema incidence is unclear, with conflicting regional reports.



WHAT THIS STUDY ADDS: This national study showed that the annual empyema-associated hospitalization rates in children increased, despite decreased rates of bacterial pneumonia and invasive pneumococcal disease. The current PCV7 is not decreasing the incidence of empyema.

abstract

OBJECTIVE: To determine if the incidence of empyema among children in the United States has changed since the introduction of the pneumococcal conjugate vaccine in 2000.

METHODS: We used the nationally representative Kids' Inpatient Database to estimate the annual total number of hospitalizations of children ≤ 18 years of age that were associated with empyema in 1997, 2000, 2003, and 2006. Using US Census data, estimated counts were converted into annual incidence rates per 100 000 children. Incidence rates were compared between 1997 and later years to determine the impact of pneumococcal conjugate vaccine on hospitalization rates.

RESULTS: During 2006, an estimated total of 2898 (95% confidence interval [CI]: 2532–3264) hospitalizations of children ≤ 18 years of age in the United States were associated with empyema. The empyema-associated hospitalization rate was estimated at 3.7 (95% CI: 3.3–4.2) per 100 000 children, an increase of almost 70% from the 1997 empyema hospitalization rate of 2.2 (95% CI: 1.9–2.5) per 100 000. The rate of complicated pneumonia (empyema, pleural effusion, or bacterial pneumonia requiring a chest tube or decortication) similarly increased 44%, to 5.5 (95% CI: 4.8–6.1) per 100 000. The rate of bacterial pneumonia decreased 13%, to 244.3 (95% CI: 231.1–257.5) per 100 000. The rate of invasive pneumococcal disease (pneumonia, sepsis, or meningitis caused by *Streptococcus pneumoniae*) decreased 50%, to 6.3 (95% CI: 5.7–6.9) per 100 000.

CONCLUSIONS: Among children ≤ 18 years of age, the annual empyema-associated hospitalization rates increased almost 70% between 1997 and 2006, despite decreases in the bacterial pneumonia and invasive pneumococcal disease rates. Pneumococcal conjugate vaccine is not decreasing the incidence of empyema. *Pediatrics* 2010;125:26–33

AUTHORS: Su-Ting T. Li, MD, MPH and Daniel J. Tancredi, PhD

Department of Pediatrics, University of California at Davis, Sacramento, California

KEY WORDS

empyema, epidemiology, heptavalent pneumococcal conjugate vaccine, pneumococcal infections, pneumonia, pneumococcal, adolescent, child, preschool, infant, retrospective studies, United States

ABBREVIATIONS

PCV7—heptavalent pneumococcal conjugate vaccine
IPD—invasive pneumococcal disease
KID—Kids' Inpatient Database
ICD-9-CM—*International Classification of Diseases, Ninth Revision, Clinical Modification*
MRSA—methicillin-resistant *Staphylococcus aureus*
CI—confidence interval

www.pediatrics.org/cgi/doi/10.1542/peds.2009-0184

doi:10.1542/peds.2009-0184

Accepted for publication Jul 9, 2009

Address correspondence to Su-Ting T. Li, MD, MPH, University of California at Davis, 2516 Stockton Blvd, Sacramento, CA 95817. E-mail: su-ting.li@ucdmc.ucdavis.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

Copyright © 2009 by the American Academy of Pediatrics

FINANCIAL DISCLOSURE: *The authors have indicated they have no financial relationships relevant to this article to disclose.*

Pneumonia is the most common cause of hospitalization of children in the United States.¹ Empyema is associated with 3% of all pneumonia hospitalizations² and up to one third of pneumococcal pneumonia hospitalizations.³ Empyema causes significant morbidity, with prolonged hospitalizations⁴⁻⁶ and multiple invasive procedures.^{4,5} *Streptococcus pneumoniae* is the most common organism responsible, causing 17% to 28% of bacterial pneumonia in the United States and up to 50% in developing countries.⁷⁻⁹

In February 2000, the heptavalent pneumococcal conjugate vaccine (PCV7) was licensed in the United States. In October 2000, the Advisory Committee on Immunization Practices recommended PCV7 for all children <2 years of age.⁹ PCV7 was designed to protect against the most common serotypes that cause invasive pneumococcal disease (IPD) (meningitis, bacteremia, and pneumonia) in children.^{9,10} Within 1 year after its introduction, the incidence of IPD had decreased across all age groups,¹¹⁻¹⁴ including those for whom the vaccine is not recommended, such as infants too young to be vaccinated,¹³ children >5 years of age,¹¹ and adults.^{11,14} Although PCV7 clearly reduced the incidence of IPD, its effect on empyema incidence was less clear. Studies of empyema incidence conducted after the introduction of PCV7 showed contradictory results: Empyema incidence was reported to have increased by 88% in Utah¹⁵ and by 400% in California¹⁶ but was shown to have decreased by 55% in Texas¹⁷ and remained unchanged in Quebec, Canada.¹⁸ These discrepancies highlight the limitations of regional studies. This study was designed to determine whether the incidence of empyema in children has changed since the introduction of PCV7 in the United States in 2000.

METHODS

Data Source

This study was a retrospective cohort analysis using administrative data from the Kids' Inpatient Database (KID) from 1997, 2000, 2003, and 2006.¹⁹ The KID is a national pediatric hospital discharge database developed by the Agency for Healthcare Research and Quality as part of the Healthcare Cost and Utilization Project and was designed to generate robust national estimates of pediatric hospitalizations.¹⁹ The KID contains a random 10% sample of all uncomplicated births and 80% of all other hospitalizations for children aged 20 years and younger from 2000, 2003, and 2006 and for children aged 18 years and younger from 1997 from each nonfederal, short-term hospital located in the participating states, with up to 15 diagnoses and 15 procedures for each hospitalization. The KID contained ~1.9 million pediatric discharges from 22 states and 2521 hospitals for 1997, ~2.5 million discharges from 27 states and 2784 hospitals for 2000, ~2.9 million discharges from 36 states and 3438 hospitals for 2003, and ~3.9 million discharges from 38 states and 3739 hospitals for 2006.

The KID contains discharge-level records of patient demographic information, diagnostic codes, procedure codes, and discharge disposition. No laboratory or physiologic patient data are included. Discharge weights provided with the KID were used to obtain national estimates.²⁰ The institutional review board at the University of California at Davis approved this study.

Patients

This study included children ≤18 years who were hospitalized in 1997, 2000, 2003, or 2006. Exclusion criteria included patients (1) born during the hospital admission, (2) transferred from another hospital, (3) transferred

from another facility (including a long-term care facility), (4) with a missing admission source, or (5) with a missing age.

Main Outcome

Children with empyema were identified by an *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) code for empyema (510.0, 510.9) in any of the diagnoses on the discharge record.^{21,22} Codes for empyema cases related to tuberculosis (012.XX) were not counted.

Data Analysis

We estimated the total number of empyema-associated hospitalizations by year of admission, both overall and within strata defined by age group and gender. Point and variance estimates for these national estimates were calculated by using the Healthcare Cost and Utilization Project's weighting methodology, as implemented in the survey data analysis procedures in version 9.1.3 of SAS/Stat Software.²⁰ US Census estimates of the total number of children ≤18 years of age were used to convert estimated counts into hospitalization rates.²³ Hospitalization rates were expressed as the number of estimated hospitalizations per 100 000 children and were assumed to be approximately normally distributed for purposes of computing confidence intervals (CIs) and assessing the statistical significance of rate comparisons. Contrasts between prevaccine (1997) and transition-year (2000) or postvaccine (2003 and 2006) rates were adjusted for the survey design and were estimated both with and without adjustment for age. To explore whether PCV7 had a greater impact on the ages for which the vaccine was intended, we (1) examined whether the mean age of empyema hospitalization increased during the time period studied and (2) performed subgroup anal-

yses restricted to children <5 years of age.

To investigate potential confounders associated with empyema incidence, we performed several additional analyses. To determine if an increase in incidence of empyema might be caused by misclassification, we examined the incidence of all complicated pneumonia in each time period. Children with complicated pneumonia were identified by ICD-9-CM codes for empyema, pleural effusion (511.1), or bacterial pneumonia (481–486) that required either chest tube placement (34.04) or a decortication procedure (34.51).

To determine if an increase in incidence of empyema might be caused by an increase in conditions that may lead to empyema, we examined the: (1) overall incidence of bacterial pneumonia and (2) incidence of microbiological causes of empyema. Because *S pneumoniae* and *Staphylococcus aureus* are the most common causes of empyema,^{8,17} we examined the incidence of both pneumococcal and *S aureus* empyema. Cases of empyema were attributed to pneumococcus if children with empyema had an additional ICD-9-CM code for pneumococcal pneumonia (481), pneumococcus (041.2), or pneumococcal septicemia (038.2). Empyema was attributed to *S aureus* if children with empyema had an additional ICD-9-CM code for *S aureus* pneumonia (482.41), *S aureus* (041.11), or *S aureus* septicemia (038.11).

In October 1997, the ICD-9-CM code for staphylococcal septicemia (038.1) was expanded to distinguish between *S aureus* septicemia (038.11), staphylococcal septicemia, and unspecified (038.10) and other (038.19) staphylococcal septicemia.²⁴ Similarly, in 1998, the ICD-9-CM coding for staphylococcal pneumonia (482.4) was expanded to distinguish between *S aureus* pneumonia (482.41), pneumonia caused by staphylococcus, and unspecified (482.40) and other (482.49) staphylococcal pneumonia.²⁴ Given the changes in ICD-9-CM coding, in case *S pneumoniae* and *S aureus* were miscoded as just streptococcus or staphylococcus, an additional sensitivity analysis was performed to examine the incidence of all streptococcus (481, 482.3, 041.2, 041.0, 038.2, 038.0) and staphylococcus (482.41, 482.40, 042.4, 041.1, 041.10, 041.11, 038.11, 038.1) empyema cases. To determine if the virulence of streptococcus or staphylococcus pneumonia had increased since 1997, we used logistic regression with empyema as the outcome variable, year as an independent categorical variable, and age and gender as potential confounders. For the year category, 1997 was used as the reference year, and 3 dummy variables were created to indicate hospitalizations from each of the years 2000, 2003, and 2006.

To verify that the impact of PCV7 on pneumococcal disease could be ascertained in the time periods studied, we examined the incidence of IPD (pneu-

mococcal bacteremia [ICD-9-CM codes 038.2 (pneumococcal septicemia) and 790.7 (bacteremia) plus 041.2 (pneumococcus)], pneumococcal meningitis (320.1), or pneumococcal pneumonia (481) in 1997, 2000, 2003, and 2006.^{9,10,12}

RESULTS

Overall

During 2006, a total of 2898 hospitalizations with empyema were estimated to have occurred among children ≤18 years of age in the United States (Table 1). The empyema hospitalization rate was 3.7 per 100 000 children, an increase of 1.5 (70%) from the 1997 rate of 2.2 per 100 000. Unless otherwise indicated, the following estimates of hospitalizations and hospitalization rates are for the year 2006. All comparisons are between 1997 and 2006.

Age and Incidence

The mean age of children hospitalized for empyema in 2006 was 6.3 years (95% CI: 5.9–6.6), 1 year younger than in 1997 (7.3 years [95% CI: 6.8–7.8]). For children <5 years of age, 1541 (95% CI: 1306–1776) empyema-associated hospitalizations were estimated, representing 53% of empyema hospitalizations among children ≤18 years old. For children <5 years old, the empyema hospitalization rate increased 100%, from 3.8 (95% CI: 3.1–4.5) in 1997 to 7.6 (95% CI: 6.4–8.7) per 100 000 children. Figure 1 shows that empyema hospitalization rates

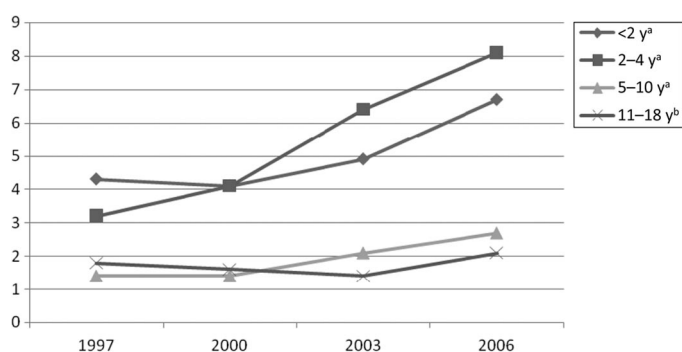
TABLE 1 Pneumonia Hospitalization Rates Among US Children ≤18 Years of Age in 1997, 2000, 2003, and 2006

Characteristic	National Estimate of Pneumonia-Associated Hospitalization Rates, n/100 000 (95% CI)				
	1997	2000	2003	2006	Rate Difference Between 1997 and 2006
Empyema	2.2 (1.9 to 2.5)	2.3 (2.0 to 2.6)	3.3 (2.8 to 3.7)	3.7 (3.2 to 4.2)	1.5 (0.9 to 2.1)
Pleural effusion	0.4 (0.3 to 0.5)	0.2 (0.2 to 0.3)	0.2 (0.2 to 0.3)	0.2 (0.1 to 0.3)	−0.2 (−0.3 to −0.1)
Bacterial pneumonia that required chest tube placement or decortication	1.3 (1.1 to 1.5)	1.4 (1.2 to 1.6)	1.6 (1.4 to 1.8)	1.6 (1.4 to 1.9)	0.33 (0.03 to 0.64)
Complicated pneumonia ^a	3.8 (3.3 to 4.2)	3.8 (3.4 to 4.3)	5.0 (4.4 to 5.5)	5.5 (4.8 to 6.1)	1.7 (0.9 to 2.4)
All bacterial pneumonia	281.1 (263.7 to 298.5)	240.2 (226.2 to 254.2)	266.8 (252.7 to 280.8)	244.3 (231.1 to 257.5)	−36.8 (−58.6 to −15.0)

^a Children with complicated pneumonia included children with empyema, pleural effusion, or bacterial pneumonia that required chest tube placement or decortication.

TABLE 2 *Streptococcus* and *Staphylococcus* Pneumonia Hospitalization Rates Among US Children ≤18 Years of Age in 1997, 2000, 2003, and 2006

Characteristic	National Estimate of <i>Streptococcus</i> - and <i>Staphylococcus</i> -Associated Pneumonia Hospitalization Rates, <i>n</i> /100 000 (95% CI)				
	1997	2000	2003	2006	Rate Difference Between 1997 and 2006
Pneumonia					
<i>S pneumoniae</i> pneumonia	8.9 (7.8 to 10.0)	4.7 (4.3 to 5.2)	4.9 (4.5 to 5.3)	4.9 (4.5 to 5.4)	−4.0 (−5.2 to −2.8)
All streptococcal pneumonia	12.6 (11.3 to 13.8)	9.1 (8.4 to 9.8)	7.8 (7.2 to 8.4)	7.8 (7.1 to 8.4)	−4.8 (−6.2 to −3.4)
Staphylococcal pneumonia	5.6 (5.0 to 6.2)	4.8 (4.0 to 5.6)	5.7 (4.9 to 6.5)	6.2 (5.4 to 7.1)	0.6 (−0.4 to 1.7)
Empyema					
<i>S pneumoniae</i> empyema	0.6 (0.4 to 0.7)	0.5 (0.4 to 0.6)	0.6 (0.5 to 0.7)	0.7 (0.5 to 0.8)	0.1 (−0.1 to 0.3)
All streptococcal empyema	0.8 (0.7 to 1.0)	0.7 (0.6 to 0.9)	0.9 (0.8 to 1.1)	0.9 (0.8 to 1.1)	0.1 (−0.1 to 0.4)
Staphylococcal empyema	0.2 (0.2 to 0.3)	0.2 (0.2 to 0.3)	0.4 (0.3 to 0.5)	0.5 (0.4 to 0.6)	0.3 (0.2 to 0.4)

**FIGURE 1**

Empyema-associated hospitalization rates per 100 000 children in 1997, 2000, 2003, and 2006. ^a $P < .01$; ^b $P = .06$.

increased for children of all age groups ($P < .01$) except children 11 to 18 years of age ($P = .06$), with the greatest increase in children 2 to 4 years of age (131%).

Complicated Pneumonias

In 2006, an estimated 4249 child hospitalizations were associated with complicated pneumonia, an increase of 45%, to 5.5 per 100 000 (Table 1). Of the children with complicated pneumonia, 68% were coded as having empyema. Although the national incidence of pleural effusion decreased, the absolute decrease was only ~120 cases of pleural effusion, far fewer than the >1200 increase in empyema incidence over the same time period.

Bacterial Pneumonia and Microbiology

The overall incidence of bacterial pneumonia decreased 13%, to 244.3 per 100 000 (Table 1). This decrease

was driven by a 29% decrease in pneumonia hospitalizations in children <2 years (-348.1 per 100 000 [95% CI: -455.7 to -240.5]); there was no decrease in bacterial pneumonia hospitalization in any other age group. Bacterial etiology was identified in 14% of pneumonias in 1997 and 12% in 2006. We noted inconsistencies for *S aureus* coding, likely secondary to introduction of specific *S aureus* ICD-9-CM codes in 1997–1998. *S aureus* accounted for 16% of staphylococcus in 1997 and 82% in 2006. Because of the inconsistency of *S aureus* coding at the species level, only genus-level results for staphylococcus are reported.

S pneumoniae (2%), other streptococcus (1%; including streptococcus, unspecified), staphylococcus (2%), and mycoplasma (3%) were the most commonly identified bacterial causes of hospitalized children with pneumonia

resulting from a specified organism, the percentage of pneumococcal pneumonia decreased from 21% to 14%; similarly, the percentage of streptococcal pneumonia decreased from 29% to 22%. The percentage of staphylococcal pneumonia increased from 12% to 16%, and the percentage attributed to other unspecified bacteria increased from 34% to 43%. The overall pneumococcal pneumonia hospitalization rate decreased 45%, to 4.9 per 100 000. There was no change in the overall staphylococcal pneumonia hospitalization rate (6.2 per 100 000).

The percentage of children hospitalized with bacterial pneumonia who had empyema increased 89%, from 0.8% in 1997 to 1.5% in 2006. The bacterial etiology was identified in 50% of empyema cases in 1997 and 43% in 2006. During this period, of children with empyema with a bacterial organism identified, the percentage of pneumococcal empyema decreased slightly, from 46% to 39%; similarly, the percentage of streptococcal empyema decreased from 66% to 56%. The percentage of staphylococcal empyema increased from 16% to 28%, and the percentage attributed to other unspecified bacteria was unchanged at ~15%. The incidence of pneumococcal empyema has not changed, with a hospitalization rate of 0.7 per 100 000. Children hospitalized with pneumococcal pneumonia were twice as likely to develop empyema in 2006 (13.7%) com-

pared with 1997 (6.4%). In the logistic regression analysis, after controlling for age and gender, children with pneumococcal pneumonia in 2006 were still twice as likely (adjusted odds ratio: 2.3 [95% CI: 1.7–3.1]) to develop empyema compared with 1997.

The incidence of staphylococcal empyema increased 135%, to 0.5 per 100 000. Children hospitalized with staphylococcal pneumonia were more likely to develop empyema in 2006 (8.7%) compared with 1997 (4.1%). In the logistic regression analysis, after controlling for age and gender, children with staphylococcal pneumonia in 2006 were still more likely (adjusted odds ratio: 2.4 [95% CI: 1.7–3.3]) to develop empyema compared with 1997.

Invasive Pneumococcal Disease

Figure 2 shows that the national incidence of IPD (pneumococcal pneumonia, bacteremia, and meningitis) decreased 50% from 1997 (12.7 per 100 000 [95% CI: 11.4–13.9]) to 2003 (6.4 [95% CI: 5.9–6.9]), and there was no additional change in IPD incidence from 2003 to 2006 (6.3 [95% CI: 5.7–6.9]). Similarly, IPD decreased 56% for children <5 years old, to 15.1 (95% CI: 13.5–16.6) per 100 000.

DISCUSSION

This study provides robust national estimates of hospitalizations associated with empyema among children in the United States. From 1997 to 2006, despite the introduction of PCV7, empyema hospitalization rates increased 70%. These increases occurred despite a decreasing incidence of bacterial pneumonia, pneumococcal pneumonia, and overall IPD, and a decreased mean age of children admitted with empyema. Specifically, we found a 45% decrease in incidence of pneumococcal pneumonia and no change in the incidence of pneumococcal empyema, making children with

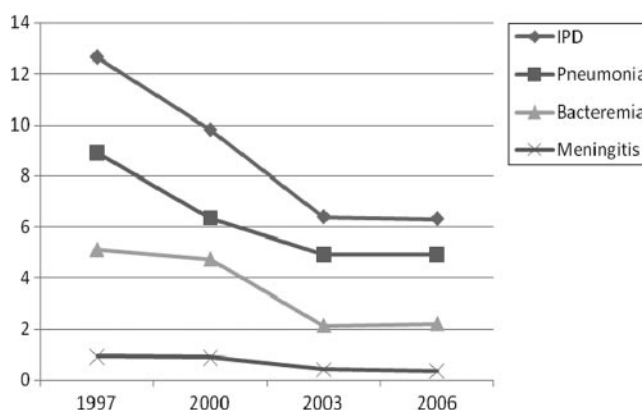


FIGURE 2

IPD hospitalization rates per 100 000 children in 1997, 2000, 2003, and 2006.

pneumococcal pneumonias twice as likely to have empyema in 2006 as in 1997. Our findings suggest that PCV7 is effective for preventing pneumonia but not effective for preventing empyema.

Before the introduction of PCV7, studies suggested that the incidence of empyema in children was increasing.^{3,17,25–34} Our study showed that despite the introduction of PCV7, the incidence of empyema in children is continuing to increase.^{15,16} The 70% increase we found in our national population-based estimates of empyema incidence reconciles the previously discrepant single-institution and regional findings,^{15–18} which may have reflected regional microbiology or referral patterns.

We found the highest increase in empyema incidence in the youngest children (<5 years old), with the highest increase in children aged 2 to 4 years. Although it is not surprising that younger children had a greater incidence of empyema than older children because pneumococcal disease disproportionately affects younger children,⁹ we do not know why children in the 2- to 4-year-old age group had a slightly higher increase in empyema incidence than the <2-year-old age group; this deserves additional study.

We found a slight decrease in overall bacterial pneumonia, driven by a 30% decrease in pneumonia in children <2

years old. These results are consistent with previous studies from which a 39% decrease in pneumonia in children <2 years old³⁵ and a trend toward a 40% decrease in pneumonia hospitalizations (including viral pneumonias) in children <1 year old.³⁶

Despite the dramatic decrease in pneumococcal pneumonia hospitalizations, we found no change in the incidence of pneumococcal empyema hospitalization. Our national results reconcile the previously discrepant regional findings, which may have reflected regional microbiology.^{17,31} Our results suggest that although PCV7 is effective against some serotypes responsible for pneumonia, it is not effective against serotypes responsible for empyema. PCV7 contains serotypes 4, 6B, 9V, 14, 18C, 19F, and 23F.^{9,10} Pneumococcal serotype 1 is responsible for only 4% to 7% of bacterial pneumonia, but is the most common cause of empyema (24%–50%)^{3,7,28,37}; it is not included in PCV7. In addition, Utah's increased empyema incidence was attributed to pneumococcal serotypes 1, 3, and 19A.¹⁵ Expanded-valency conjugate vaccines under development include a 10-valent vaccine, which additionally contains serotypes 1, 5, and 7F, and a 13-valent vaccine, which additionally contains serotypes 1, 3, 5, 6A, 7F, and 19A.

That staphylococcus pneumonia incidence was unchanged but staphylococcus empyema incidence increased may be a result of increasing methicillin-resistant *S aureus* (MRSA). This theory is supported by a Texas study that revealed an increase in the proportion of empyema cases due to *S aureus* from 18% to 60%, with 78% being caused by MRSA.¹⁷

The 50% decrease in IPD we report is consistent with the 29% to 69% decrease in IPD reported previously^{11,13} and a trend toward a 50% decrease in pneumococcal bacteremia reported in a smaller national hospital discharge survey study.³⁸ Our results are somewhat smaller than the 73% decrease in IPD in children <5 years old reported by the Active Bacterial Core Surveillance,^{39,40} which included laboratory data from both inpatient and outpatient sources, including children with occult pneumococcal bacteremia or pneumonia who may never be hospitalized.

There are some limitations in this study. Misclassification is possible in an administrative data set. Although pleural effusions may have been miscoded as empyema, the decreased number of pleural effusions (~120) was not enough to account for the additional empyema cases (>1200). Complicated pneumonias (empyemas, pleural effusions, and pneumonias requiring chest tube or decortication) also increased, although it is possible that a temporal trend toward greater intervention for children with pneumonia might lead to bias. Because the KID

does not include laboratory data such as culture results and serotyping, bacterial diagnosis must rely on coding. No studies have validated microbiology coding for children with pneumonia.

Our results, that 43% to 50% of children with empyema had a specific bacterial organism identified, are consistent with the 32% to 53% reported previously, which suggests that if specific organisms were identified, they were coded.^{7,9,17,28,33,41} Similarly, our finding that 14% of children with pneumonia had a bacterial etiology identified is consistent with the 6.5% reported in previous studies.⁷ The increased incidence of culture-negative empyema is consistent with the results of previous studies^{16,17} and may be the result of increased antibiotic pretreatment.¹⁶ This increased incidence of culture-negative empyemas may mean that we underestimated the actual increase in streptococcal empyema because previous molecular studies have found that 70% to 88% of culture-negative empyemas are caused by *S pneumoniae*, with 34% to 60% being serotype 1.^{42,43} The KID is only available every 3 years, which limits the ability to evaluate year-to-year variation. However, we were able to examine 4 years of data (1997, 2000, 2003, and 2006), which show that empyema incidence has continued to increase. It is possible that changes from 1997 to 2006 in the set of states included in the KID to make it more nationally representative may have influenced the empyema rates reported.

Finally, the KID does not provide immunization status. We were unable to test whether children who received PCV7 were less likely to have IPD or empyema. However, in the United States, among children born in 2001, 89% received ≥ 1 dose and 68% received ≥ 3 doses of PCV7, and among children born in 2005, 95% received ≥ 1 dose and 84% received ≥ 3 doses of PCV7.¹⁰ In addition, previous studies showed a decrease in IPD by 2001,¹¹ indicating that PCV7 was affecting IPD within 1 year of its introduction. Our study also revealed a decrease in IPD, indicating that although PCV7 is effective at preventing IPD, it is less effective at preventing empyema.

CONCLUSIONS

Despite the effectiveness of PCV7 in reducing pneumococcal meningitis, bacteremia, and pneumonia, the incidence of empyema has continued to increase. This is likely the result of serotype replacement with nonvaccine serotypes,^{44–47} such as serotype 1, which are more likely to cause empyema, and increasing MRSA. Because empyema incidence is increasing, not only should expanded-valency pneumococcal conjugate vaccines include serotypes currently responsible for empyema, but empyema microbiology surveillance should continue to monitor for serotype replacement.

ACKNOWLEDGMENTS

We thank Robert Byrd, MD, MPH, for thoughtful critique of this manuscript.

REFERENCES

- Elixhauser A. Hospital stays for children, 2006. In: *Statistical Brief #56: Healthcare Cost and Utilization Project*. Rockville, MD: Agency for Healthcare Research and Quality; 2008
- Clark JE, Hammal D, Spencer D, Hampton F. Children with pneumonia: how do they present and how are they managed? *Arch Dis Child*. 2007;92(5):394–398
- Tan TQ, Mason EO Jr, Wald ER, et al. Clinical characteristics of children with complicated pneumonia caused by *Streptococcus pneumoniae*. *Pediatrics*. 2002;110(1):1–6
- Li ST, Gates RL. Primary operative management for pediatric empyema: decreases in hospital length of stay and charges in a national sample. *Arch Pediatr Adolesc Med*. 2008;162(1):44–48
- Shah SS, DiCristina CM, Bell LM, Ten Have T, Metlay JP. Primary early thoracoscopy and reduction in length of hospital stay and additional procedures among children with complicated pneumonia: results of a multicenter retrospective cohort study. *Arch Pediatr Adolesc Med*. 2008;162(7):675–681
- Kozak LJ, DeFrances CJ, Hall MJ. National Hospital Discharge Survey: 2004 annual summary with detailed diagnosis and pro-

- cedure data. National Center for Health Statistics. *Vital Health Stat.* 2006;13(162)
7. Byington CL, Spencer LY, Johnson TA, et al. An epidemiological investigation of a sustained high rate of pediatric parapneumonic empyema: risk factors and microbiological associations. *Clin Infect Dis.* 2002;34(4): 434–440
 8. Rudan I, Boschi-Pinto C, Biloglav Z, Mulholland K, Campbell H. Epidemiology and etiology of childhood pneumonia. *Bull World Health Organ.* 2008;86(5):408–416
 9. Advisory Committee on Immunization Practices. Preventing pneumococcal disease among infants and young children. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep.* 2000;49(RR-9):1–35
 10. Invasive pneumococcal disease in children 5 years after conjugate vaccine introduction: eight states, 1998–2005. *MMWR Morb Mortal Wkly Rep.* 2008;57(6): 144–148
 11. Whitney CG, Farley MM, Hadler J, et al. Decline in invasive pneumococcal disease after the introduction of protein-polysaccharide conjugate vaccine. *N Engl J Med.* 2003;348(18): 1737–1746
 12. Kaplan SL, Mason EO Jr, Wald ER, et al. Decrease of invasive pneumococcal infections in children among 8 children's hospitals in the United States after the introduction of the 7-valent pneumococcal conjugate vaccine. *Pediatrics.* 2004;113(3):443–449
 13. Poehling KA, Talbot TR, Griffin MR, et al. Invasive pneumococcal disease among infants before and after introduction of pneumococcal conjugate vaccine. *JAMA.* 2006; 295(14):1668–1674
 14. Lexau CA, Lynfield R, Danila R, et al. Changing epidemiology of invasive pneumococcal disease among older adults in the era of pediatric pneumococcal conjugate vaccine. *JAMA.* 2005;294(16):2043–2051
 15. Byington CL, Korgenski K, Daly J, et al. Impact of the pneumococcal conjugate vaccine on pneumococcal parapneumonic empyema. *Pediatr Infect Dis J.* 2006;25(3): 250–254
 16. Hendrickson DJ, Blumberg DA, Joad JP, Jhavar S, McDonald RJ. Five-fold increase in pediatric parapneumonic empyema since introduction of pneumococcal conjugate vaccine. *Pediatr Infect Dis J.* 2008;27(11): 1030–1032
 17. Schultz KD, Fan LL, Pinsky J, et al. The changing face of pleural empyemas in children: epidemiology and management. *Pediatrics.* 2004;113(6):1735–1740
 18. De Wals P, Robin E, Fortin E, et al. Pneumonia after implementation of the pneumococcal conjugate vaccine program in the province of Quebec, Canada. *Pediatr Infect Dis J.* 2008;27(11):963–968
 19. HCUP Kids' Inpatient Database (KID). Healthcare Cost and Utilization Project (HCUP). 1997, 2000, 2003, and 2006. Agency for Healthcare Research and Quality, Rockville, MD. Available at: www.hcup-us.ahrq.gov/kidoverview.jsp. Accessed October 16, 2009
 20. Chu B, Houchens R, Elixhauser A, Ross D. Using the KIDS' Inpatient Database (KID) to Estimate Trends. HCUP Methods Series Report # 2007-02 Online. January 10, 2007. U.S. Agency for Healthcare Research and Quality. Available at: www.hcup-us.ahrq.gov/reports/2007_02.pdf. Accessed October 16, 2009
 21. National Center for Health Statistics (NCHS) and the Centers for Medicare and Medicaid Services. *ICD-9-CM: International Classification of Diseases, 9th Revision, Clinical Modification.* 9th ed. Salt Lake City, UT: Medicode; 2008
 22. Centers for Disease Control and Prevention, National Center for Health Statistics. Conversion table of new ICD-9-CM Codes, October 2009 Available at: www.cdc.gov/nchs/data/icd9/icd9cnv10.pdf. Accessed October 16, 2009
 23. US Census Bureau. US Census Bureau population estimates. Available at: www.census.gov/popest/national/national.html. Accessed October 16, 2009
 24. Centers for Disease Control and Prevention, National Center for Health Statistics. Conversion table of new ICD-9-CM Codes, October 2008; 2008
 25. Finley C, Clifton J, Fitzgerald JM, Yee J. Empyema: an increasing concern in Canada. *Can Respir J.* 2008;15(2):85–89
 26. Gupta R, Crowley S. Increasing paediatric empyema admissions. *Thorax.* 2006;61(2): 179–180
 27. Playford SD, Smyth AR, Stewart RJ. Increase in incidence of childhood empyema. *Thorax.* 1997;52(10):932
 28. Fletcher M, Leeming J, Cartwright K, Finn A. Childhood empyema: limited potential impact of 7-valent pneumococcal conjugate vaccine. *Pediatr Infect Dis J.* 2006;25(6): 559–560
 29. Rees JH, Spencer DA, Parikh D, Weller P. Increase in incidence of childhood empyema in West Midlands, UK. *Lancet.* 1997; 349(9049):402
 30. Roxburgh GS, Youngson GG. Childhood empyema in North-East Scotland over the past 15 years. *Scott Med J.* 2007;52(4):25–27
 31. Byington CL, Samore MH, Stoddard GJ, et al. Temporal trends of invasive disease due to *Streptococcus pneumoniae* among children in the intermountain west: emergence of nonvaccine serogroups. *Clin Infect Dis.* 2005;41(1):21–29
 32. Spencer DA, Iqbal SM, Hasan A, Hamilton L. Empyema thoracis is still increasing in UK children. *BMJ.* 2006;332(7553):1333
 33. Alfaro C, Fergie J, Purcell K. Emergence of community-acquired methicillin-resistant *Staphylococcus aureus* in complicated parapneumonic effusions. *Pediatr Infect Dis J.* 2005;24(3):274–276
 34. Roxburgh CS, Youngson GG, Townend JA, Turner SW. Trends in pneumonia and empyema in Scottish children in the past 25 years. *Arch Dis Child.* 2008;93(4): 316–318
 35. Grijalva CG, Nuorti JP, Arboğast PG, et al. Decline in pneumonia admissions after routine childhood immunisation with pneumococcal conjugate vaccine in the USA: a time-series analysis. *Lancet.* 2007;369(9568): 1179–1186
 36. Nelson JC, Jackson M, Yu O, et al. Impact of the introduction of pneumococcal conjugate vaccine on rates of community acquired pneumonia in children and adults. *Vaccine.* 2008;26(38):4947–4954
 37. Eastham KM, Freeman R, Kearns AM, et al. Clinical features, aetiology and outcome of empyema in children in the north east of England. *Thorax.* 2004;59(6):522–525
 38. Shah SS, Ratner AJ. Trends in invasive pneumococcal disease-associated hospitalizations. *Clin Infect Dis.* 2006;42(1):e1–e5
 39. Centers for Disease Control and Prevention. Active Bacterial Core Surveillance Report, Emerging Infections Program Network, *Streptococcus pneumoniae*, 2006. Available at: www.cdc.gov/abcs/surveillance/spneu06.pdf. Accessed October 16, 2009
 40. Centers for Disease Control and Prevention. Active Bacterial Core Surveillance Report, Emerging Infections Program Network, *Streptococcus pneumoniae*, 1997. Available at: www.cdc.gov/abcs/surveillance/spneu07.pdf. Accessed October 16, 2009
 41. Nyambat B, Kilgore PE, Yong DE, et al. Survey of childhood empyema in Asia: implications for detecting the unmeasured burden of culture-negative bacterial disease. *BMC Infect Dis.* 2008;8:90
 42. Tarragó D, Fenoll A, Sanchez-Tatay D, et al. Identification of pneumococcal serotypes from culture-negative clinical specimens by novel real-time PCR. *Clin Microbiol Infect.* 2008;14(9):828–834
 43. Eltringham G, Kearns A, Freeman R, et al. Culture-negative childhood empyema is

- usually due to penicillin-sensitive *Streptococcus pneumoniae* capsular serotype 1. *J Clin Microbiol.* 2003;41(1):521–522
44. Lipsitch M. Bacterial vaccines and serotype replacement: lessons from *Haemophilus influenzae* and prospects for *Streptococcus pneumoniae*. *Emerg Infect Dis.* 1999;5(3):336–345
 45. Mera R, Miller LA, Fritsche TR, Jones RN. Serotype replacement and multiple resistance in *Streptococcus pneumoniae* after the introduction of the conjugate pneumococcal vaccine. *Microb Drug Resist.* 2008;14(2):101–107
 46. Lipsitch M, O'Neill K, Cordy D, et al. Strain characteristics of *Streptococcus pneumoniae* carriage and invasive disease isolates during a cluster-randomized clinical trial of the 7-valent pneumococcal conjugate vaccine. *J Infect Dis.* 2007;196(8):1221–1227
 47. Singleton RJ, Hennessy TW, Bulkow LR, et al. Invasive pneumococcal disease caused by nonvaccine serotypes among Alaska native children with high levels of 7-valent pneumococcal conjugate vaccine coverage. *JAMA.* 2007;297(16):1784–1792

Chronic Traumatic Encephalopathy: A 2008 Rand Corp. study reports an increase in blast injuries to our armed forces in Iraq or Afghanistan. According to an article in The New York Times (Schwarz A, The New York Times, June 23, 2009), the reason for this are the improvements in armor and in our medical treatments resulting in improved survival for those who experience a serious blast exposure. Yet the impact of repeated pressure variations in the brain from these explosions is not without its own complications—similar to the repeated brain trauma experienced by football players and boxers. The result is a disorder referred to as chronic traumatic encephalopathy or CTE, characterized by memory loss, possible depression and dementia that can occur in the 30's or 40's when someone is exposed to repeated blast injuries, rather than later in life. One wonders whether military personnel who experience post-traumatic stress disorder after being exposed to combat and repeated blast injuries have physical brain damage to accompany this psychological disorder. If your young adult patients enlist and are sent to areas where explosions are ongoing, it is a good idea to keep CTE on your differential if their mood dramatically changes upon their return home.

Noted by JFL, MD

ERRATA

Li S-TT and Tancredi DJ. Empyema Hospitalizations Increased in US Children Despite Pneumococcal Conjugate Vaccine. *Pediatrics*. 2010;125(1):26–33

An error occurred in this article by Li et al, published in the January 2010 issue of *Pediatrics* (doi:10.1542/peds.2009-0184). On page 23, under the Methods section in the Abstract, the first sentence reads “We used the nationally representative Kids’ Inpatient Database to estimate the annual total number of hospitalizations of children \geq 18 years of age that were associated with empyema in 1997, 2000, 2003, and 2006.” This should have read: “We used the nationally representative Kids’ Inpatient Database to estimate the annual total number of hospitalizations of children \leq 18 years of age that were associated with empyema in 1997, 2000, 2003, and 2006.”

doi:10.1542/peds.2009-3496

Senserrick T, Ivers R, Boufous S, Chen H-Y, Norton R, Stevenson M, van Beurden E, and Zask A. Young Driver Education Programs That Build Resilience Have Potential to Reduce Road Crashes. *Pediatrics*. 2009;124(5):1287–1292

An error occurred in this article by Senserrick et al. published in the November 2009 issue of *Pediatrics* (doi:10.1542/peds.2009-0659). On page 1288, under the heading Driver Education Programs, on line 41-44, reads: “Additional details can be on the program Web site (www.ryda.com.au/html/the-program.html.)” This statement has been retracted. The program operators advise that this is a different program from that evaluated at the time of the study.

doi:10.1542/peds.2009-3582

PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Empyema Hospitalizations Increased in US Children Despite Pneumococcal Conjugate Vaccine

Su-Ting T. Li and Daniel J. Tancredi

Pediatrics 2010;125;26; originally published online November 30, 2009;

DOI: 10.1542/peds.2009-0184

The online version of this article, along with updated information and services, is located on the World Wide Web at:

</content/125/1/26.full.html>

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2010 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™



Empyema Hospitalizations Increased in US Children Despite Pneumococcal Conjugate Vaccine

Su-Ting T. Li and Daniel J. Tancredi

Pediatrics 2010;125;26; originally published online November 30, 2009;

DOI: 10.1542/peds.2009-0184

Updated Information & Services	including high resolution figures, can be found at: /content/125/1/26.full.html
References	This article cites 37 articles, 14 of which can be accessed free at: /content/125/1/26.full.html#ref-list-1
Citations	This article has been cited by 29 HighWire-hosted articles: /content/125/1/26.full.html#related-urls
Post-Publication Peer Reviews (P³Rs)	One P ³ R has been posted to this article: /cgi/eletters/125/1/26
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): Infectious Disease /cgi/collection/infectious_diseases_sub
Errata	An erratum has been published regarding this article. Please see: /content/125/2/415.1.full.html
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: /site/misc/Permissions.xhtml
Reprints	Information about ordering reprints can be found online: /site/misc/reprints.xhtml

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2010 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

