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The Changing Face of Pleural Empyemas in Children: Epidemiology and Management

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The Changing Face of Pleural Empyemas in Children: Epidemiology and Management

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ABSTRACT. *Objective.* **Empyema remains a significant cause of morbidity in children. This study evaluates the changes that have affected the outcome in children with pleural empyema, including the emergence of resistant organisms, the introduction of the pneumococcal conjugate vaccine, and earlier treatment with video-assisted thoracoscopy (VATS).**

Methods. **A retrospective chart review was performed on all patients who were discharged with a diagnosis of empyema and community-acquired pneumonia over a 10-year period (1993–2002) at Texas Children's Hospital in Houston, Texas. Data collected included demographic information, clinical presentation, radiographic studies, laboratory data including culture results, and hospital course.**

Results. **A total of 230 charts were available for review. The mean age of the patients was 4.0 ± 3.6 years. Of the pleural fluid cultures performed, 32% (69 of 219) were positive. An additional 27 patients had a cause identified by blood culture. The first penicillin-nonsusceptible *Streptococcus pneumoniae* was identified in 1995, and the first methicillin-resistant *Staphylococcus aureus* was identified in 1998. After the universal use of the pneumococcal conjugate vaccine, 3 major changes have occurred (1999–2000 vs 2001–2002): 1) the number of patients admitted with empyema (per 10 000 admissions) has decreased from 23 to 12.6; 2) the prevalence of *S pneumoniae* has decreased from 66% (29 of 44) to 27% (4 of 15); and 3) *S aureus* has become the most common pathogen isolated (18% vs 60%), with 78% of those being methicillin resistant. The use of early VATS (<48 hours after admission) versus late VATS (>48 hours after admission) significantly decreased the length of hospitalization (11.49 ± 6.56 days vs 15.18 ± 8.62 days).**

Conclusions. **The microbiologic cause of empyema has changed with an increasing incidence of *S aureus*, particularly methicillin-resistant *S aureus*. The use of VATS for initial therapy of empyema results in decreased duration of fever and length of hospitalization.** ***Pediatrics* 2004;113:1735–1740; *empyema, community-acquired pneumonia, video-assisted thoracic surgery, children, microbiology.***

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ABBREVIATIONS. CTD, chest tube drainage; VATS, video-assisted thoracic surgery; PCN-NS, penicillin nonsusceptible; MIC, minimum inhibitory concentration; LOS, length of stay; MRSA, methicillin-resistant *Staphylococcus aureus*; PCN-S, penicillin susceptible; MSSA, methicillin-susceptible *Staphylococcus aureus*.

Pleural effusions and empyemas are known complications of bacterial pneumonia. Effusions occur in at least 40% of bacterial pneumonias, with up to 60% of effusions resulting in the formation of empyema in all age groups.[1,2] Recent studies have noted an increase in the incidence of empyemas in children.[3–6] Other reports have suggested a change in the cause of empyemas in children, including an increase in resistant organisms as well as a decline in the incidence of *Streptococcus pneumoniae*.[7–10]

Multiple nonantibiotic treatment modalities exist for pleural effusions and empyemas, including thoracentesis, chest tube drainage (CTD), instillation of fibrinolytic therapy into the pleural cavity, and decortication. With the advent of video-assisted thoracic surgery (VATS), pleural debridement, or "limited decortication," has become more common. The less invasive nature of VATS, as well as excellent published results, has led many experts to recommend an early surgical approach to drain the pleural space, rather than thoracentesis, chest tube placement, or antibiotics alone.[11,12] This study was performed to document the changes in microbiologic causes and therapeutic procedures during the past 10 years in patients with empyema associated with community-acquired pneumonia at Texas Children's Hospital.

METHODS

Medical records of all patients who were discharged with a diagnosis of empyema associated with community-acquired pneumonia from 1993 to 2002 from Texas Children's Hospital in Houston, Texas, a tertiary referral hospital, were reviewed retrospectively. Cases were identified through *International Classification of Diseases, Ninth Revision* codes of 510.0 (empyema with fistula) or 510.9 (empyema without fistula). Coding of the diagnosis of empyema was at the discretion of the discharge physician. The annual number of patients admitted was obtained from the Information Services Department. For our study, an empyema was defined as a loculated or septated effusion by radiographic study or findings of pus or loculated effusion at the time of surgical intervention. Patients were excluded when they had significant neurologic abnormalities predisposing to aspiration, immunosuppression, or a significant underlying disease that would not be associated with community-acquired pathogens (eg, tracheostomy, cystic fibrosis).

Organisms defined as pathogens included *S pneumoniae*, *Staph-*

ylococcus aureus, group A streptococcus, and *Haemophilus influenzae*. Penicillin-nonsusceptible (PCN-NS) *S pneumoniae* was defined as a penicillin minimum inhibitory concentration (MIC) ≥0.1 μg/mL, penicillin-intermediate MIC >0.1 to 1.0 μg/mL, and penicillin-resistant MIC ≥2 μg/mL by E-test. Duration of fever was defined as the length of time until the patient was afebrile (<100.5°F) for 24 hours. Length of hospitalization was defined as the number of days that the patient was hospitalized at our institution.

A standardized data form was completed retrospectively for each patient with empyema. Information collected included demographic, preadmission, microbiologic, radiographic, management, and complication data. The study was approved by the Institutional Review Board of Baylor College of Medicine. Data were entered in to a Microsoft Access (Redmond, WA) database. Data analysis was performed with Minitab (State College, PA) statistical software. Analysis of covariance was used to assess the effects of VATS timing and differences between resistant and susceptible bacteria on length of stay (LOS) and length of fever while adjusting for potential confounding variables. χ^2 was used to compare incidence rates over time. Results are presented as mean ± standard deviation. A *t* test was used to compare baseline characteristics of the early versus late VATS intervention groups.

RESULTS

A total of 230 charts were reviewed. A complete analysis could not be performed on 18 charts. However, limited data were available through the hospital computer system (demographic data, laboratory and culture data, and radiographic data). Procedure data were not available on these patients. The average age of the 230 patients was 4.0 ± 3.6 years (range: 3 weeks to 16.6 years). The male to female ratio was 1.3:1. The ethnic breakdown was similar to that of overall admissions to the hospital except that significantly more white children were admitted with empyema compared with overall hospital admissions ($P < .05$).

During the study period, the number of admissions for empyema initially increased, with a peak of 23.0 cases/10 000 admissions during 1999–2000 ($P = .06$ for 1997–1998 vs 1999–2000, and $P = .007$ for 1993–1998 vs 1999–2000). However, the number of cases decreased during the following 2-year period (12.6 cases/10 000 admissions; $P = .06$) to a similar rate to that seen in 1997–1998 (Table 1). Of the pleural fluid cultures performed, 32% (69 of 219) were positive. An additional 27 patients had a cause identified by blood culture (overall yield: 43%). There were no positive blood cultures for *S aureus* during the study period. The number of positive cultures did not significantly change during the 10-year study period. However, there was a significant decrease in the proportion of positive cultures during the last 2-year period (44 [50%] of 88 in 1999–2000 and 15 [32%] of 47 in 2001–2002; $P = .04$; Table 1).

The first PCN-NS *S pneumoniae* was identified in 1995, and the first methicillin-resistant *S aureus* (MRSA) was identified in 1998. The number of *S pneumoniae* cases also increased during the first 8 years of the study, with a peak incidence of 29 cases/44 isolates in 1999–2000. During 2001–2002, the number of cases of *S pneumoniae* decreased significantly (4 cases/15 isolates; $P = .03$). The absolute number of cases of empyema caused by *S aureus* increased substantially during the entire period of the study, although the proportion of isolates that were *S aureus* did not change significantly (χ^2 for trend, $P = .09$) However, the proportion of cases caused by *S aureus* increased significantly during 1999–2000 versus 2001–2002 (8 of 44 vs 9 of 15; $P = .03$; Table 1, Fig 1). The percentage of PCN-NS *S pneumoniae* did not change significantly during the study period. Thirteen of 52 pneumococcal isolates were resistant to erythromycin; only 4 of 52 isolates were resistant to clindamycin. Among the positive cultures, the proportion that was MRSA increased significantly during the course of the study ($P = .00016$, χ^2 for trend). The number of cases of empyema based on causative organism and age is presented in Fig 2. The empyema cases caused by *S aureus* occurred primarily in children who were younger than 1 year (14 *S aureus* isolates/28 positive cultures for children younger than 1 year vs 10 *S aureus* isolates/197 positive culture for children older than 1 year; $P < .001$).

The LOS was not significantly different between the patients with infection caused by PCN-NS *S pneumoniae* versus penicillin-susceptible (PCN-S) *S pneumoniae* (8.92 ± 1.31 days vs 9.64 ± 1.42 days; $P = .158$). However, it did approach significance when corrected for age with the PCN-S *S pneumoniae* group having a longer LOS (14.70 ± 2.18 days vs 20.88 ± 2.42 days; $P = .07$). In contrast, comparing empyema cases caused by MRSA versus methicillin-susceptible *S aureus* (MSSA), the MRSA group had a significantly longer LOS (18.83 ± 1.66 days vs 14.00 ± 1.66 days; $P = .05$). Duration of fever was similar in the PCN-NS versus PCN-S *S pneumoniae* (8.92 ± 1.31 days vs 9.64 ± 1.42 days; $P = .71$) groups as well as the MRSA versus MSSA (7.10 ± 1.55 days vs 10.09 ± 1.47 days; $P = .18$) groups.

Information on therapeutic interventions was available for 212 patients. Of those, 4 received antibiotics only, 19 had a thoracentesis and/or had a chest tube placed, and 189 underwent some type of surgical intervention: VATS ($n = 125$), minithora-

TABLE 1. Culture Data Based on Time Period

	1993–1994	1995–1996	1997–1998	1999–2000	2001–2002	*P* Value*
Total admissions for empyema	19	24	48	88	51	
Empyema admissions/10 000 hospital admissions	5.8	6.7	13	23	12.6	.06
Proportion of positive cultures (blood or pleural fluid)	7/19	8/15	20/48	44/88	15/47	.04
S pneumoniae isolates	5	3	11	29	4	.03
PCN-NS *S pneumoniae* isolates	0	2	4	11	2	NS
S aureus isolates	1	3	3	8	9	.03
MRSA isolates	0	0	1	4	7	NS

NS indicates not significant.
* *P* value compares 1999–2000 and 2001–2002.

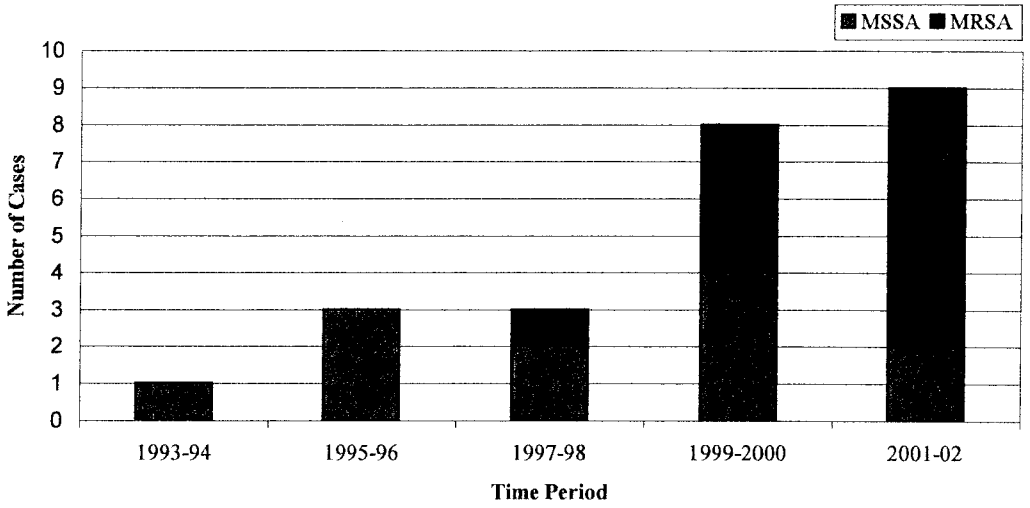

Fig 1. Number of cases of empyema caused by *S aureus* from 1993 to 2002 at Texas Children's Hospital. MSSA versus MRSA.

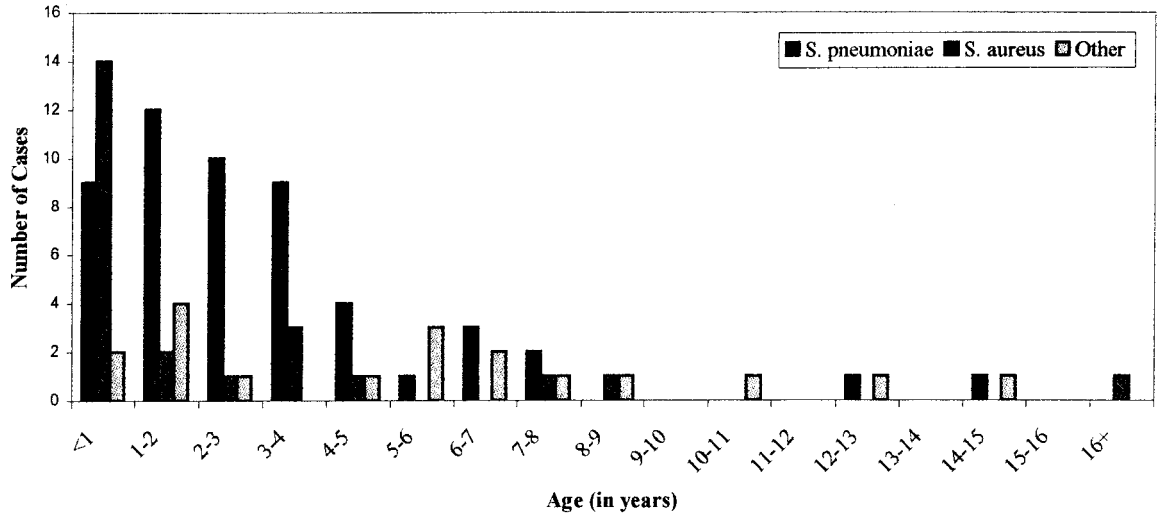

Fig 2. Distribution of empyema cases based on age and cause from 1993 to 2002 at Texas Children's Hospital.

cotomy (n = 31), or open thoracotomy (n = 32). Complications, including lung abscess, pneumatocele formation, bronchopleural fistula formation, respiratory failure, requirement of a blood transfusion, and air leak >24 hours, were not statistically significant between the nonsurgical and surgical groups. Eight patients required lobectomy during the study period. There were no deaths from empyema associated with community-acquired pneumonia during the study period.

A total of 125 patients underwent VATS. Of those, 49 patients had the procedure performed within 48 hours of admission (early VATS) versus 76 who underwent the procedure >48 hours after admission (late VATS). Baseline characteristics of the 2 groups are presented in Table 2. The only significant differences were previous hospitalization and admission service, with more patients in the early intervention group being admitted to the surgical service. The LOS was significantly shorter in the early VATS group compared with the late VATS group (11.49 ± 6.56 days vs 15.18 ± 8.62 days; P = .008). Adjustment for age, race, gender, admission service, fever, and cough duration before hospitalization, duration of presumed viral illness before hospitalization, attendance at child care, smoking in the home, use of nonsteroidal anti-inflammatory agents and antibiotics before hospitalization, bacterial cause, and previous hospitalization both individually and combined did not alter the significance of the decreased LOS in the early intervention group (11.12 ± 2.82 days vs 13.94 ± 2.74 days; P = .013). The length of fever after

TABLE 2. LOS and Baseline Characteristics of Early Versus Late VATS

	Early VATS	Late VATS	*P* Value
LOS (all patients)	11.49 ± 6.56	15.18 ± 8.62	.008
Age	5.01 ± 4.23	3.78 ± 3.24	NS
Admission service, %			.04
General pediatrics	51	67	
Pulmonary	26	20	
Surgery	12	1	
Other	10	12	
LOS (Texas Children's Hospital admission only)	9.91 ± 2.95	12.34 ± 2.80	.027

hospitalization was significantly shorter for early versus late VATS (7.1 ± 5.6 days vs 9.4 ± 5.5 days; $P = .046$). Forty-five percent of patients in the early VATS group remained febrile on day 5, with 10% still febrile on day 15 (Fig 3). There were no significant differences in complication rates between the early and late VATS groups, including lung abscess, pneumatocele formation, bronchopleural fistula formation, respiratory failure, requirement of a blood transfusion, air leak >24 hours, and need for lobectomy (Table 3).

TABLE 3. Complications for Early Versus Late VATS

	Early ($n = 46$)	Late* ($n = 79$)
Lung abscess	3	4
Pneumatocele	2	7
Bronchopleural fistula	1	1
Respiratory failure (before or after procedure)	5	6
Blood transfusion	9	18
Air leak >24 h	3	5
Lobectomy	3	3

* There were no significant differences found.

DISCUSSION

Pneumonia is a common childhood disease. with an incidence of between 1.0 and 4.5 cases per 100 children per year.[13] Although most cases of pneumonia are viral in cause, bacteria are the causative agent in 20% to 30% of patients.[14] Bacterial pneumonia can be severe and life-threatening, accounting for ~3 million pediatric deaths per year worldwide, primarily in resource-poor countries.[15] Our study confirms the observations of others that there has been an increase in the incidence of empyema in children.[3–6] However, the routine administration of the pneumococcal conjugate vaccine to infants beginning at 2 months of age has resulted in a significant decrease in the number of cases of empyema caused by *S pneumoniae*. This observation affirms the recent findings of Whitney et al[16] indicating a decrease in the incidence of invasive pneumococcal disease among children in the United States after universal vaccination. Our study also confirms the findings of Byington et al[6] with an increased rate of admission of white children in patients with empyema compared with the general hospital population. The reason for this increase is unclear; however, it may be attributable to better access of care by white children who are treated with inadequate outpatient therapy.

Identification of the causative agent in children with empyema is often difficult, necessitating the use of empiric rather than specific therapy.[13,14] Reported diagnostic yield from pleural and/or blood cultures ranges from 60% to 70%.[6,17] Only 43% of our pediatric patients had a cause established by either blood or pleural cultures. Campbell et al[18] suggested that blood cultures have limited usefulness in adults with community-acquired pneumonia. Our yield from blood cultures was higher before 2001, with a large decrease in the incidence of positive blood cultures during the past 2 years, related both to a decline in pneumococcal infections and to an increase in the incidence of *S aureus* empyema that was associated with negative blood cultures. However, in patients with a positive culture, 28% had a cause identified by blood culture only.

The most common pathogens that cause effusions or empyemas associated with community-acquired pneumonia in children are *S pneumoniae*, *S aureus*, and group A streptococcus.[2] From 1995 to 1998, there was a significant increase in the proportion of *S pneumoniae* isolates resistant to penicillin, cefotaxime, erythromycin, and trimethoprim-sulfamethoxazole recovered from invasive infections in the United States. Multidrug resistance also increased.[9] Patients who were at an increased risk of having *S pneumoniae* isolates with antibiotic resistance were younger than 5 years, of white race, or hospitalized.[9] However, multiple studies have not demonstrated an increase in adverse outcomes of pneumonia caused by PCN-NS versus PCN-S *S pneumoniae*. Hardie et al[8] demonstrated no difference in the LOS, days of fever,

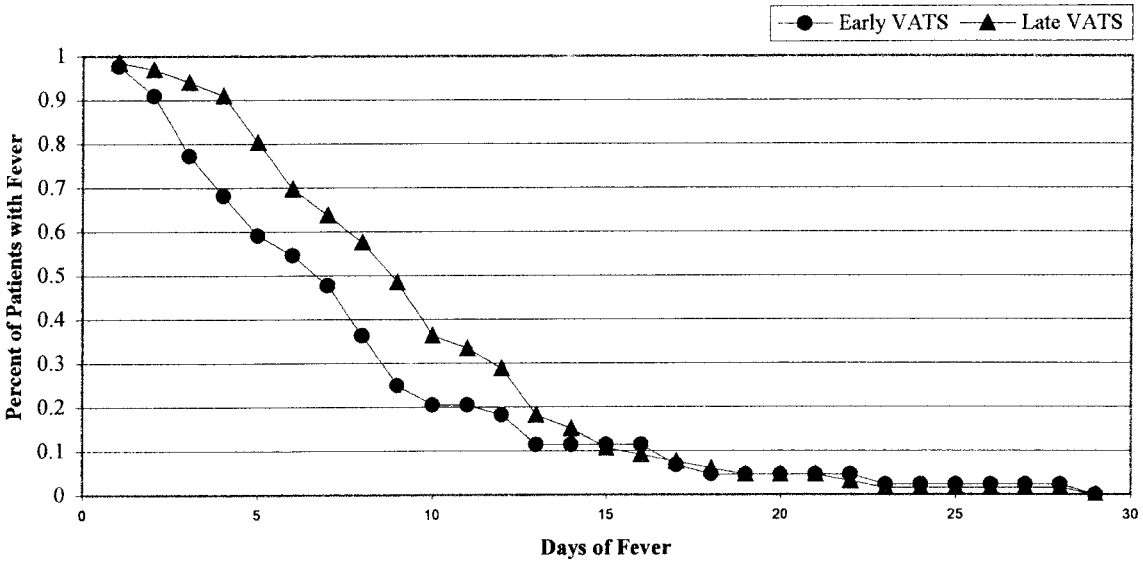

Fig 3. Proportion of patients with empyema becoming afebrile in early versus late VATS.

days of hypoxia, or need for lobectomy between these 2 groups. Furthermore, Tan et al[10] showed no difference in the development of complicated versus uncomplicated effusions with PCN-S versus PCN-NS *S pneumoniae*. In fact, Byington et al[6] found an increase in the percentage of PCN-NS organisms in patients with simple pneumonia as compared with those who developed an empyema.

During 1999–2000, there was an increase in the number of cases of *S pneumoniae* at our institution. However, our data from the 2001–2002, which follows the initiation of routine use of the pneumococcal conjugate vaccine, demonstrate a significant decrease in the number of cases of empyema caused by *S pneumoniae.* We found no significant difference in the LOS or duration of fever in the PCN-NS and PCN-S groups of *S pneumoniae*, with a trend toward a longer LOS in the PCN-S group. We did find a low rate of resistance of *S pneumoniae* to clindamycin, suggesting that this antibiotic may be a useful option in the treatment of pneumonia caused by PCN-NS *S pneumoniae*. Buckingham et al[19] recently demonstrated an increase in the number of cases of complicated parapneumonic effusions caused by *S aureus*; however, they only accounted for 30% of the overall cases. Our absolute number of cases of empyema caused by *S aureus* has increased during the 10 years of the study; the proportion of cases of empyema caused by *S aureus* has significantly increased during the last 4 years of the study. *S aureus* has now become the most common causative agent of empyema identified in our institution. The majority of these isolates are MRSA (78% in 2001–2002).

The LOS for patients with empyema caused by MRSA was significantly longer than for those with pneumonia caused by MSSA; however, the duration of fever was similar in the 2 groups. Empiric therapy of empyema and pleural effusions associated with community-acquired pneumonia should cover MRSA in communities in which at least 10% of community *S aureus* isolates are MRSA. Vancomycin is the gold standard therapy for treating serious infections caused by MRSA. Clindamycin is a valuable agent for treating less severe pneumonia/empyema caused by susceptible community-acquired MRSA isolates, but the laboratory must screen for the inducible form of macrolide-lincosamide-streptogramin resistance.[20]

The management of empyema in children remains controversial. The use of antibiotics alone is effective therapy in patients with simple pneumonia and those with early effusion. However, drainage of the pleural space is often necessary in later stages of parapneumonic effusions and empyemas. Nonsurgical methods to drain the pleural space include thoracentesis, single or repeated; small-caliber, flexible drainage catheters; and large-bore CTD, with or without the use of fibrinolytics.[21–28] Historically, CTD has been the mainstay of therapy; however, the other methods are gaining favor. Thoracentesis is generally easy to perform and can provide information on the causative agent as well as be therapeutic. Historically, surgical debridement or decortication in patients with empyema has been reserved for those with disease refractory to medical management. However, as early as 1990, some authorities advocated early surgical intervention in the treatment of empyema, especially in patients with severe disease.[12] With the increased use of the minimally invasive surgery in the mid-1990s, VATS has been proposed as a first-line therapy in patients with empyema, especially those with more advanced disease. A number of retrospective reviews have demonstrated that VATS decreases the length of CTD and hospitalization.[11,12,29,30] One study demonstrated not only a shorter LOS but also a decrease in the cost of hospitalization in patients who were treated with primary VATS.[31]

In our institution, most of the children who require a thoracostomy tube are taken to the operating room for placement under more controlled and less psychologically traumatic circumstances. In the past several years, VATS has been generally performed in these patients as they were usually placed under general anesthesia. In the past 10 years, the majority of our patients (189 of 212) have had surgical intervention at some point in their hospital course. Therefore, it is impossible for us to compare conservative management (ie, antibiotics ± thoracentesis/chest tube) with antibiotics plus surgical intervention. However, of the 125 patients who underwent VATS, those who were treated earlier (within 48 hours of admission) had a significantly shorter LOS. The only significant baseline differences between these 2 groups were previous hospitalization and admission service, with more patients in the early intervention group being admitted to the surgical service. Because length of hospitalization before admission at our hospital was not taken into account in calculating LOS, the additional days of hospitalization could bias the total length of hospitalization of these patients transferred to our hospital and thus affect the difference between these 2 groups. However, there was no significant interaction between LOS and previous hospitalization on analysis. When the LOS was corrected for previous hospital admissions ($n = 43$ patients), it remained significantly shorter for patients who were treated with early VATS (Table 2). The 4-day reduction in hospitalization that we observed is clinically significant, especially in the current era of managed care. Patients who underwent early VATS also had a decreased length of fever overall. However, although most patients in the early VATS group were afebrile by day 5, 10% remained febrile on day 15, with 1 patient febrile on day 28. Therefore, persistently febrile patients should be watched closely with no additional intervention unless there is a change in the patient's status. On the basis of our results, we believe that early VATS is an effective and safe method of treating empyema in children and should be considered a treatment of choice.

In summary, the bacterial cause of empyema in children is changing. Since the routine administration of the pneumococcal conjugate vaccine, we have seen a significant decrease in the number of cases of empyema caused by *S pneumoniae* and, for reasons that are not clear, an increase in the number of cases

caused by *S aureus*, with the majority being MRSA. Clindamycin should adequately cover both MRSA and PCN-NS *S pneumoniae* in almost all outpatient instances. Either clindamycin or vancomycin should be included in the regimen of inpatients, the specific choice depending on the severity of illness. Early intervention with VATS seems to decrease the length of hospitalization and should be considered for patients with empyema.

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