



Clinical experience of managing empyema thoracis in children

Fang-Liang Huang¹, Po-Yen Chen¹, Jui-Shan Ma¹, Hsiu-Wen Yu¹, Kun-Chia Lu⁴, Ching-Shiang Chi¹,
Yeu-Jun Lau², Hai-Chyi Peng³

¹Department of Pediatrics; ²Section of Infectious Diseases, Department of Medicine; ³Division of Pediatric Surgery, Taichung Veterans General Hospital; and ⁴Department of Pediatrics, Cheng Ching Hospital, Taichung, Taiwan, ROC

Received: June 7, 2001 Revised: August 16, 2001 Accepted: September 11, 2001

Data of 54 children with a diagnosis of thoracic empyema at a medical center in central Taiwan from January 1991 through April 2001 were analyzed. Their mean age was 4.4 years and the mean hospital stay was 13 days. *Streptococcus pneumoniae* was the most common pathogen, followed by *Staphylococcus aureus* and *Haemophilus influenzae*. These patients were divided into 2 groups according to the treatment method. Twenty-two patients were treated successfully with antibiotics and tube thoracostomy, whereas the other 32 children required further pleural decortication with antibiotic treatment. In patients with empyema, decortication allowed for more rapid defervescence than did closed tube thoracostomy (1.94 vs 5.04 days; $p < 0.001$) and there were no complications in the group that underwent decortication treatment ($p < 0.03$). In conclusion, the decortication of loculated empyema thoracis in children is a safe and effective management procedure.

Key words: Decortication, empyema, *Streptococcus pneumoniae*

Thoracic empyema, a collection of purulent material in the pleural space, occurs when bacteria in pleural fluid create products of infection that prevent full expansion of the lungs. It progresses through 3 phases, typically over a 3- to 4-week period. Phase 1 is an exudative phase with thin fluid and few cells; the second phase is a fibrinopurulent phase with large quantities of white cells and fibrin, resulting in loculations and a limiting membrane forming around the lung; and the third phase is an organizing phase with fibroblasts growing into the exudate, producing an inelastic membranous "peel" that encases the lung [1]. Although its incidence and mortality are low, pediatric empyema can be associated with considerable morbidity [2,3]. The optimal management remains controversial, with advocates for a variety of treatment options, which include antibiotics alone or in combination with thoracocentesis, tube thoracostomy, fibrinolytic agents, thoracoscopy, minithoracotomy, debridement, and decortication [4]. Surgical intervention increase of thoracic empyema is usually reserved for patients who do not respond to conservative management consisting of prolonged antibiotic therapy and chest tube drainage. Many recent reports have attempted to identify the role

of thoracostomy and decortication in the management of children's empyema [5,6].

The Taichung Veterans General Hospital (TVGH) is a tertiary referral center. Most children with thoracic empyema who are unresponsive to antimicrobial agents with or without chest tube drainage are referred to TVGH. Most of them present with a prolonged fever. A progressive surgical evaluation via chest ultrasound and computed tomography (CT) assisted in deciding on the best procedure to reduce treatment time. The objective of this study is to evaluate the effectiveness of surgical intervention in managing empyema thoracis in children.

Patients and Methods

We reviewed the medical records of children younger than 14 years who were admitted to TVGH with empyema and parapneumonic effusion during the period from January 1991 through April 2001. Patients presenting with pneumonia (characterized by fever, cough, chest pain, rales, decreased breathing sound, and leukocytosis) were initially evaluated by using chest radiograph. Patients who were diagnosed as having lobar or lobular pneumonia by chest radiograph with or without pleural effusion were further evaluated by chest ultrasound scan to differentiate between consolidative pneumonia and loculated thoracic empyema, except for some patients with obvious loculated empyema. A pediatric surgeon was consulted

Corresponding author: Dr. Po-Yen Chen, Department of Pediatrics, Taichung Veterans General Hospital, 160, Section 3, Chung-Kang Road, Taichung 407, Taiwan, ROC. E-mail: pychen@vghtc.vghtc.gov.tw

for further surgical evaluation in patients considered having empyema. A chest CT scan was performed to confirm the loculations of empyema and to make a surgical evaluation. Most of the patients initially received chest tube drainage or simple needle thoracocentesis, except for those who were going to receive surgical treatment. Antibiotics were given empirically after diagnosis for treatment of community-acquired pneumonia and were shifted to suitable drugs later according to the microorganism culture and sensitivity results. Pleura decortication was performed when the parapneumonic effusion was either encased by a thick peel, multiloculated, or refractory to medical management. Thoracic empyema is defined as loculated lesions in the pleural space with a pleural peel formation visible on a chest ultrasound or CT scan; pleural effusion that contained white blood cells of more than 1000/ μ L or from which organisms could be cultured; or exudative, fibrosis debris noted in the pleural tissue pathology [4]. A diagnosis of thoracic empyema was initially made on the basis of clinical examination, chest radiography, ultrasound, and/or CT scan and was further confirmed by the pleural fluid cultures and analysis or surgical findings (purulent content peel formation, necrotizing change). Confirmed empyema cases that were transferred from other hospitals with chest tube intubation were included in this study. Those patients

with underlying lung disease, extrapulmonary complications, or iatrogenic pulmonary infection were excluded from this study.

A retrospective review of medical records included patients' demographics, clinical presentation, chest tube drainage, type of surgical intervention, duration of fever, biochemical and microbial studies of pleural effusion, and radiographic evaluation. Patients were divided into 2 groups. Group 1 is comprised of patients who received conservative management (antibiotics with or without chest tube drainage), and Group 2, those who received conservative treatment as well as further decortication or a thoracotomy.

Statistical analysis

Statistical significance was analyzed by using Student's *t* test, Fisher's exact test, or chi-square analysis. The statistical software used is Sigma Plot 4.0 software (SPSS, Chicago, IL, US). A *p* value less than 0.05 was considered statistically significant.

Results

Of the 61 children treated for thoracic empyema at TVGH during a 10-year period (1991-2001), 54 were included in this study. Seven patients were excluded due to other complications—one patient with septic arthritis, 2 with meningitis, 2 with iatrogenic esophageal

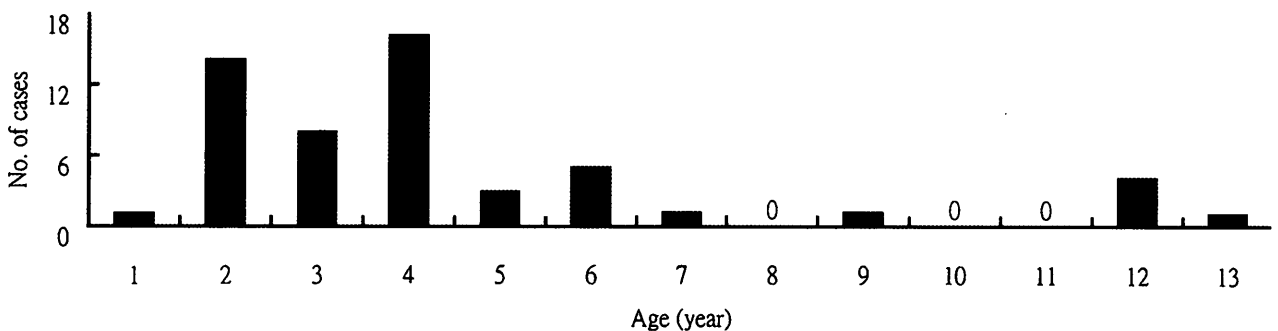


Fig. 1. Age distribution of patients with thoracic empyema.

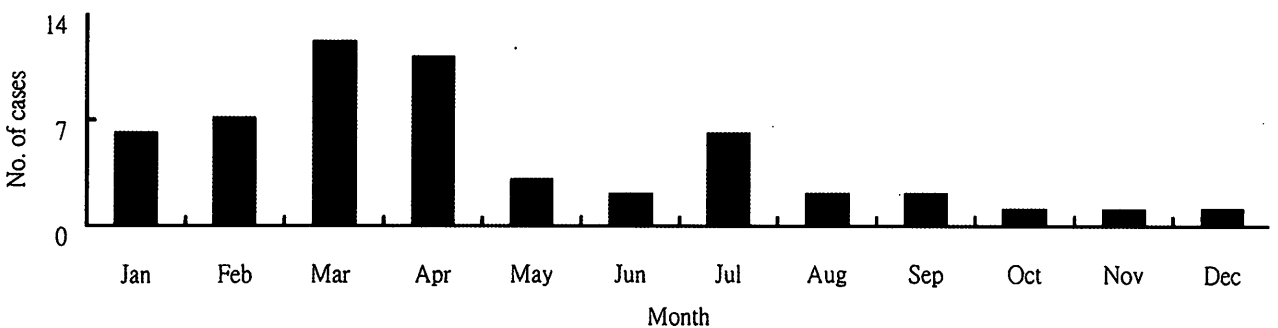


Fig. 2. Seasonal distribution of patients with thoracic empyema (1991-2001).

Table 1. Demographics, image study and outcome of 54 children with thoracic empyema

Category	Total n = 54 (%)	Group 1 n = 22 (%)	Group 2 n = 32 (%)	<i>p</i>
Mean age (year)	4.4 ± 3.08	4.88 ± 3.13	4.13 ± 2.92	NS
Sex ratio (M:F)	28:26	12:10	16:16	NS
Duration of hospital stay (day)	13.07 ± 4.86	12.13 ± 5.06	13.72 ± 4.67	NS
Time to afebrile after admission (day)	4.46 ± 4.12	5.77 ± 4.56	3.56 ± 3.59	NS
Time to afebrile after procedure (day)	3.20 ± 3.62	5.04 ± 4.64	1.94 ± 1.93	<0.001
Duration of chest tube placement (day)	7.19 ± 3.27	6.56 ± 2.56	7.50 ± 3.57	NS
Transferred from other hospitals	35 (64.8)	10 (45.4)	25 (78.1)	0.01
Chest computed tomography scan	37 (68.5)	8 (36.4)	29 (90.6)	<0.01
Chest ultrasound	50 (92.5)	19 (86.4)	31 (96.8)	NS
Complication ^a	3 (5.6)	3 (13.6)	0	0.03

Abbreviation: NS = non-significant

^aLung cyst formation

Note: Group 1 = patients who received conservative management; Group 2 = patients who received conservative treatment as well as operation

perforation with empyema, one with underlying biliary atresia, and one with cerebral palsy. Thirty-two (59.3%) patients received antibiotic treatment and pleural decortication at TVGH, whereas 22 (40.7%) were managed by conventional antimicrobial therapy with or without simple chest tube drainage. In the operative therapy group, all patients' conditions were compatible with the definition of thoracic empyema in exudative pleural effusion or fibrosis in pleural tissue pathology. In the conservative therapy group, 16 patients received chest tube insertion, 2 patients received simple needle thoracocentesis and 4 were given a diagnosis of thoracic empyema based on image study and clinical findings. Group 2 included 10 patients who were transferred from other hospitals with chest tube insertions for further surgical evaluation. All of them had received broad-spectrum antibiotic treatment and chest tube drainage,

but a persistent fever was noted.

The mean age of the patients was 4.4 years (range, 0.8-13 years), and 70.3% of patients were 2 to 4 years old (Fig. 1). The male-to-female ratio was 1.08:1 (28 boys and 26 girls). Among the patients, 66.7% were admitted in the early spring between January and April (Fig. 2). The difference in the mean age, sex ratio, duration of hospital stay, total fever days after admission, time afebrile after receiving chest tube insertion or decortication operation, and duration of chest tube placement between the 2 groups were compared (Table 1). There was no statistical difference except for total fever days after management procedure performed at this hospital. The management procedure was thoracocentesis or chest tube insertion or image diagnosis for Group 1, and decortication for Group 2. Prolonged fever (mean, >5 days) was the most common

Table 2. Blood and pleural effusion microorganism culture and laboratory analysis in patients with thoracic empyema

	Total n = 54 (%)	Group 1 n = 22 (%)	Group 2 n = 32 (%)	<i>p</i>
Blood culture (+)	6 (11.1)	2 (9.1)	4 (12.5)	NS
Pleural effusion culture (+)	23 (42.6)	10 (45.5)	13 (40.6)	NS
Blood or serum		NS		
White blood cell (/μL)	21226 ± 10790	19235 ± 10100	22574 ± 11191	NS
Neutrophil (%)	75.7 ± 14.0	77.5 ± 13.4	74.5 ± 14.6	NS
C-reactive protein (mg/dL)	18.3 ± 11.7	18.9 ± 11.8	17.8 ± 11.8	NS
Pleural effusion				NS
White blood cell (/μL)	21702 ± 36319	17302 ± 25650	25611 ± 44109	NS
Neutrophil (%)	77.26 ± 18.87	73.8 ± 20.2	80.0 ± 17.8	NS
LDH (μ/L)	9136.48 ± 19659.9	4840.5 ± 6466.5	13179.7 ± 26419.6	NS
Protein (g/dL)	4.4 ± 0.84	4.16 ± 0.76	4.59 ± 0.86	NS
Sugar (mg/dL)	46.6 ± 40.4	62.1 ± 44.2	32.7 ± 31.5	0.015

Abbreviations: LDH = lactate dehydrogenase; NS = non-significant

Note: Group 1 = patients who received conservative management; Group 2 = patients who received conservative treatment as well as operation

Table 3. Clinical symptoms and signs in patients with thoracic empyema

Symptom/sign	Total n = 54 (%)	Group 1 n = 22 (%)	Group 2 n = 32 (%)	p
Fever	54 (100)	22 (100)	32 (100)	NS
Cough	51 (94.4)	22 (100)	29 (90.6)	NS
Decrease breathing sound	48 (88.9)	16 (72.8)	32 (100)	<0.01
Dyspnea	17 (31.5)	10 (45.5)	7 (21.9)	NS
Chest pain	15 (27.8)	8 (36.4)	7 (21.9)	NS
Rales	25 (46.3)	11 (50.0)	14 (43.8)	NS
Rhonchi	20 (37.0)	11 (50.0)	9 (28.1)	NS
GI tract symptom ^a	11 (20.3)	1 (4.5)	8 (25.0)	0.03
Lung location (R/L side)	23 (42.6)/31 (57.4)	12 (54.5)/10 (45.5)	11 (34.3)/21 (65.6)	NS

Abbreviations: GI = gastrointestinal

^aVomiting and/or abdominal pain

Note: Group 1 = patients who received conservative management; Group 2 = patients who received conservative treatment as well as operation

problem of those who received conventional management (16 patients with chest tube drainage). Those who received surgical decortication had their fever subside very quickly (mean, <2 days). More than 60% of these patients were referred from other hospitals due to the failure of clinical treatment with persistent fever, which was most common clinical presentation (78.1%) in Group 2. The surgical conditions were evaluated by using chest CT (68.5%) and/or chest ultrasound (92.5%), especially in Group 2. There were no deaths in this study. Complications such as lung cysts were found in 3 cases in Group 1, but none in Group 2. The patients with lung cyst formation were all excluded from further surgical treatment after the initial clinical evaluation including image studies, and only one received diagnostic pleural effusion tapping. They received antibiotic treatment and their clinical condition improved gradually. Lung cyst formation was noted in the follow-up chest image examination.

There were no statistical differences in results of blood or pleural effusion laboratory analysis except for the sugar levels in the pleural effusion between the 2 groups (Table 2). The most common clinical features

were fever (54/54, 100%), cough (51/54, 94.4%), decreased breathing sound (48/54, 88.9%), rales (25/54, 46.3%), rhonchi (20/54, 37%), dyspnea (17/54, 31.5%), chest pain (15/54, 27.8%), and gastrointestinal tract symptoms (abdominal pain and vomiting, 11/54, 20.3%) (Table 3). There were more patients with decreased breathing sound and gastrointestinal symptoms in Group 2. There was no significant difference in the location of thoracic empyema. A definitive bacteriological diagnosis was confirmed in 25 (46.3%) of 54 patients. Nineteen children had positive pleural fluid culture results only, 4 had both positive pleural fluid and blood culture results, and another 2 had positive blood culture results only. Six patients with positive blood culture results all revealed *Streptococcus pneumoniae*, and 4 of them have culture results compatible with pleural effusion culture. The results of the pleural effusion cultures are shown in Table 4. *S. pneumoniae* was the bacterial pathogens responsible for 68% (17/25) of the cases.

Discussion

Lower respiratory tract infections in children were complicated by parapneumonic fluid collections in 50% to 94% of cases, but this usually resolves itself spontaneously after the pneumonia recedes [7]. One in every 155 cases of pneumonia progresses to established empyema, according to the report by Chonmaitree and Powell [8]. The development of empyema marks an important change in the morbidity and mortality of the pneumonic process [9]. Therefore, thoracic empyema remains a relatively common problem in the pediatric population. In this study, the high prevalence (66.7%) of thoracic empyema during the late winter and early spring (from January to April) may coincide with a higher incidence of common viral upper airway

Table 4. Microorganisms isolated from pleural effusion in patients with thoracic empyema (n = 23)

Microorganism	No. of patients (%)
<i>Streptococcus pneumoniae</i>	13 (56.5)
<i>Staphylococcus aureus</i>	3 (13)
<i>Haemophilus influenzae</i>	2 (8.7)
<i>Escherichia coli</i>	1 (4.3)
<i>Streptococcus</i> sp.	1 (4.3)
<i>Acinetobacter</i> sp.	1 (4.3)
Mixed ^a	2 (8.7)

^a*S. pneumoniae* with *S. aureus* and *S. pneumoniae* with *Peptostreptococcus* sp.

infections, which are usually followed by bacterial invasion of the throat colonist. The severity of the disease can relate to the virulence of the etiological bacteria, the integrity of the specific host defense, and the course of management. Otherwise, age was one of the risk factors of thoracic empyema in this study, which was comparable to other research [10]. The majority of the patients in this study were between 2 and 6 years old, an age group marked by its higher prevalence of pneumonia [11].

Thoracic empyema is always induced by bacterial infection; however, a definitive bacteriological finding is usually difficult. The bacterial isolation rate from parapneumonic fluid or blood samples ranges from 30% to 78.8% (with a mean of 50%) [2,4,6-8,12-16]. *S. pneumoniae* is the most common etiology of childhood community-acquired pneumonia and thoracic empyema, which accounts for 1% to 13.8% of pneumonia [17] and is even more common in children with thoracic empyema [12]. A bacterial etiology was identified from bacterial culture in 25 (46.3%) of 54 cases in this study. The TVGH is a referral center in central Taiwan and most (64.8%) of these patients were transferred from other hospitals with partial or failed treatment, including antibiotics alone or in combination with chest tube drainage. This may have contributed to the relatively low bacterial isolation rate in comparison with other series. The microorganism identification rate can be improved by using an antigen test, which provides an indirect proof even though antibiotics have already been administered [2]. In this study, the most common bacterial pathogen was *S. pneumoniae* (31.5%), followed by *Staphylococcus aureus* (7.4%) and *Haemophilus influenzae* (3.7%), a finding comparable to other studies [12,13]. The mortality rate of *S. pneumoniae* pneumonia ranges from 0.5% to 12% in the literature [17].

There are 3 rapid stages of thoracic empyema, beginning with an initial exudative state, moving to a fibrinopurulent state and progressing finally to the lobulated organizational state. This progression may take about 1 to 4 weeks from the onset of an initial pleural effusion [14]. Antimicrobial therapy with or without chest tube drainage remains the main choice of treatment in the early stage of thoracic empyema [10,18]. In children, thoracic empyema may progress more rapidly, even when appropriate antibiotics are administered [4]. Recent studies emphasize the importance of aggressive treatment of thoracic empyema to avoid further organizational formation [4-6,18-22]. The advantage of immediate surgical intervention of thoracic empyema includes a rapid

remission of fever, rapid re-expansion of the lung, and a reduction in the duration of hospital stay [18]. The objective is to prevent long-term lung damage. Early surgical intervention by thoracostomy with decortication has been advocated by many investigators, when traditional management does not result in a prompt clinical resolution [2,4-6,19-22]. Early surgical intervention facilitates the removal of restrictive purulent debris, decreases further parenchymal injury, and promotes rapid recovery [15]. This study corroborates the approach. In this series, 59.3% of children with thoracic empyema received surgical management, including thoracoscopic and thoracotomy decortication. The majority of patients were transferred to TVGH for further surgical evaluation and most (78.1%) of them received decortication management. This may account for the high percentage in comparison with other reports of 16% to 35% decortication in pediatric patients [12,13,16,19], excluding the study of Shanker *et al* [4] that found an 80% decortication. There has been a recent resurgence of interest in the early use of fibrinolytic agents (streptokinase or urokinase) to avoid the progression to loculated empyema [14,23-25]. However, these agents were not used in this study, as most of them were admitted with late-stage empyema, especially those transferred from other hospitals, which makes this form of management less effective.

Carey *et al* [18] suggested that the method of treatment should be based on radiological staging and clinical status. In addition to chest X-ray, thoracic CT and ultrasound scan are valuable tools for evaluating the pathological process in thoracic empyema, and for providing suitable methods for planning treatment [4,5,18]. Ultrasound scans were performed in 92.6% of patients in this study, which provided a good visualization of the loculations and its internal content of lesions. Ultrasound scan was especially useful for an accurate chest tube insertion. A chest CT was performed in 68.5% of patients, which delineates the extent of parenchymal and pleural disease, as well as the extent of loculation and pleural peel formation. A suggested clinical indication for surgical intervention includes persistent fever, persistent respiratory distress, persistent leukocytosis, persistent systemic toxicity [2], and perhaps, progressive thrombocytosis [26,27]. Surgical management evaluation simply from the clinical symptoms or laboratory analysis is not suggested. However, a decreased breathing sound and gastrointestinal symptoms, including abdominal pain or vomiting, were statistically more common in Group 2 than in Group 1 (Table 3). The glucose concentration

of pleural effusion was significantly lower in Group 2 (Table 2), which indicates a more advanced or severe empyema [19].

Patients who received pleural decortication defervesced much more rapidly than those who were treated with a chest tube alone (Table 1) ($p < 0.001$). A lower complication rate also was noted ($p < 0.03$). Previous reports showed mean durations of hospital stay for the traditional treatment of children with thoracic empyema of 16 to 74 days [6,10,19,22]. With an aggressive surgical approach, the mean hospital stay was reduced to between 6.8 and 11 days [2,6,7,22]. In this study, the mean duration of hospital stay was 13.07 days, no matter how serious the disease. Fever is an important clinical presentation in empyema thoracis, and those with complicated empyema always have a prolonged fever course. Early surgical pleural decortication allowed for more rapid defervescence.

In conclusion, *S. pneumoniae* is the major bacterial pathogen of thoracic empyema in children in central Taiwan, and pleural decortication is a good therapeutic modality. The advantages of this procedure are low morbidity and mortality rates with rapid defervescence. In our experience, pleural decortication has proved to be a safe and effective treatment for children with thoracic empyema.

References

- Andrews NC, Parker EF, Shaw RR, Wilson NJ, Webb WR. Management of nontuberculous empyema. *Am Rev Respir Dis* 1962;85:935-6.
- Khakoo GA, Goldstraw P, Hansell DM, Bush A. Surgical treatment of parapneumonic empyema. *Pediatr Pulmonol* 1996;22:348-56.
- Campbell PW III. New developments in pediatric pneumonia and empyema. *Curr Opin Pediatr* 1995;7:278-82.
- Shankar KR, Kenny SE, Okoye BO, Carty HM, Lloyd DA, Losty PD. Evolving experience in the management of empyema thoracis. *Acta Paediatr* 2000;89:417-20.
- Rizalar R, Somuncu S, Bernary F, Arıturk E, Gunaydin M, Gurses N. Postpneumonic empyema in children treated by early decortication. *Eur J Pediatr Surg* 1997;7:135-7.
- Eren N, Ozcelic C, Ener BK, Ozgen G, Solak H, Balci AE, Tas S. Early decortication for postpneumonic empyema in children. *Scand J Thor Cardiovasc Surg* 1995;29:125-9.
- Merry CM, Bufo AJ, Shah RS, Schropp KP, Lobe TE. Early definitive intervention by thoracoscopy in pediatric empyema. *J Pediatr Surg* 1999;34:178-80.
- Chonmaitree T, Powell KR. Parapneumonic pleural effusion and empyema in children: review of a 19-year experience 1962-1980. *Clin Pediatr* 1983;22:414-9.
- Himelamn RB, Callen PW. The prognostic value of loculation in parapneumonic pleural effusions. *Chest* 1986;90:852-6.
- McLaughlin FJ, Goldmann DA, Rosenbaum DM, Harris GB, Schuster SR, Strieder DJ. Empyema in children: clinical course and long-term follow up. *Pediatr* 1984;73:587-93.
- Jacobs NM, Haris VJ. Acute *Haemophilus pneumoniae* in childhood. *Am J Dis Child* 1979;133:603-5.
- Hardie W, Bokulic R, Garcia VF, Reising SF, Christie CD. Pneumococcal pleural empyemas in children. *Clin Infect Dis* 1996;22:1057-63.
- Doski JJ, Lou D, Hicks BA, Megison SM, Sanchez P, Contidor M, Guzzetta PC. Management of parapneumonic collections in infants and children. *J Pediatr Surg* 2000;35:265-8.
- Steinbrecher HA, Najmaldin AS. Thoracoscopy for empyema in children. *J Pediatr Surg* 1998;33:708-10.
- Stovroff M, Teague G, Heiss KF, Parker P, Ricketts RR. Thoracoscopy in the management of pediatric empyema. *J Pediatr Surg* 1995;30:1211-5.
- Chan W, Keyser-Gauvin E, Davis GM, Nguyen LT, Laberge JM. Empyema thoracis in children: a 26-year review of the Montreal Children's Hospital experience. *J Pediatr Surg* 1997;32:870-2.
- Ma JS, Chen PY, Chi CS, Lin JF, Lau YJ. Invasive *Streptococcus pneumoniae* infection of children in central Taiwan. *J Microbiol Immunol Infect* 2000;33:169-75.
- Carey JA, Hamilton JR, Spencer DA, Gould K, Hasan A. Empyema thoracis: a role for open thoracotomy and decortication. *Arch Dis Child* 1998;79:510-3.
- Hoff SJ, Neblett WW, Edwards KM, Heller RM, Pietsch JB, Holcomb GW Jr, Holcomb GW 3rd. Parapneumonic empyema in children: decortication hastens recovery in patients with severe pleural infections. *Pediatr Infect Dis J* 1991;10:194-9.
- Foglia RP, Randolph J. Current indications for decortication in the treatment of empyema in children. *J Pediatr Surg* 1987;22:28-33.
- Hoover EL, Hsu HK, Ross MJ, Gross AM, Webb H, Ketosugbo A, Finch P. Reappraisal of empyema thoracis, surgical intervention when the duration of illness is unknown. *Chest* 1986;90:511-5.
- Kercher KW, Attorri RJ, Hoover JD, Morton D. Thoracoscopic decortication as first-line therapy for pediatric parapneumonic empyema: a case series. *Chest* 2000;118:24-7.
- Kornecki A, Sivan Y. Treatment of loculated pleural effusion with intrapleural urokinase in children. *J Pediatr Surg* 1997;32:1473-5.
- Rosen H, Nadkarni V, Theroux M, Padman R, Klein J. Intrapleural streptokinase as adjunctive treatment for persistent empyema in pediatric patients. *Chest* 1993;103:1190-3.
- Krishnan S, Amin N, Dozor AJ, Stringel G. Urokinase in the management of complicated parapneumonic effusion in children. *Chest* 1997;112:1579-83.
- Wolach B, Morag H, Drucker M, Sadan N. Thrombocytosis after pneumonia with empyema and other bacterial infections in children. *Pediatr Infect Dis J* 1990;9:718-21.
- Yokoyama A, Maruyama M, Ito M, Kohno N, Hiwada K, Yano S. Interleukin 6 activity in pleural effusion, its diagnostic value and thrombopoietic activity. *Chest* 1992;102:1055-9.