CHEST®

Official publication of the American College of Chest Physicians

Interventional Management of Pleural Infections

John E. Heffner, Jeffrey S. Klein and Christopher Hampson

The online version of this article, along with updated information and services can be found online on the World Wide Web at:
http://chestjournal.chestpubs.org/content/136/4/1148.full.html

AMERICAN COLLEGE OF CHEST PHYSICIANS®

Interventional Management of Pleural Infections

John E. Heffner, MD, FCCP; Jeffrey S. Klein, MD, FCCP; and Christopher Hampson, MD

Pleural infections represent an important group of disorders that is characterized by the invasion of pathogens into the pleural space and the potential for rapid progression to frank empyema. Previous epidemiologic studies have indicated that empyema is increasing in prevalence, which underscores the importance of urgent diagnosis and effective drainage to improve clinical outcomes. Unfortunately, limited evidence exists to guide clinicians in selecting the ideal drainage intervention for a specific patient because of the broad variation that exists in the intrapleural extent of infection, presence of locules, comorbid features, respiratory status, and virulence of the underlying pathogen. Moreover, many patients experience delays in both the recognition of infected pleural fluid and the initiation of appropriate measures to drain the pleural space. The present review provides an update on the pathogenesis and interventional therapy of pleural infections with an emphasis on the unique role of image-guided drainage with small-bore catheters. *(CHEST 2009; 136:1148–1159)*

Abbreviations: ACCP = American College of Chest Physicians; BTS = British Thoracic Society; MIST1 = Multicenter Intrapleural Sepsis Trial; rtPA = recombinant tissue plasminogen activator; US = ultrasonography; VATS = video-assisted thoracoscopic surgery

Infections of the pleural space present in a highly variable manner and affect a heterogeneous population of patients with diverse underlying etiologic conditions (Table 1). All pleural infections, however, share in common a considerable potential for death and lifelong morbidity.[1,2] Most case series[2–6] have reported mortality rates between 7% and 33%, with mortality rates at > 50% among elderly patients with comorbidities.[2,6–8] More recent epidemiologic studies[9,10] have indicated that empyema has increased in incidence during the last 2 decades. Hospital discharge data in Washington state demonstrate an increase in the empyema incidence rate by 2.8% per year from 1987 to 2004.[9] Similar data show a 12.4% age-adjusted increase in the empyema incidence rate in Canada from 1995 to 2003, which affected mostly children and the elderly.[10] An aging population, longer survival times for immunocompromised patients and those with comorbid diseases, and changing virulence of pleural pathogens[11,12] suggest that these incidence trends will continue.

Because of the considerable mortality and morbidity associated with pleural infections, experts recommend[13] adherence to modern principles of empyema management that promote early diagnosis and prompt pleural drainage. Delays in initiating effective drainage prolong hospital stays, increase the likelihood that more invasive drainage procedures will be required, and increase mortality and morbidity.[3,14,15] Unfortunately, studies[3,14,15] have demonstrated that physicians commonly delay diagnosis and drainage for patients with pleural infections. These delays occur because no clinical features or laboratory studies clearly identify which patients with pneumonia have pleural infections. Consequently, every patient who is at risk for pleural

Community-acquired and health-care-associated pneumonia
Bronchial obstruction from tumor or foreign body
Ruptured lung abscess
Bronchiectasis
Thoracic and abdominal surgery
Chest and abdominal trauma
Thoracic interventional procedures, such as thoracentesis and esophagoscopy
Primary pleural infection from hematogenous spread
Extension of infection from neck, abdomen, or mediastinum

infections should undergo an initial evaluation to detect pleural fluid, determine the likelihood that the fluid is infected, and ensure prompt drainage when indicated.

The present review summarizes the pathophysiologic principles of empyema formation, classification and staging systems for empyema, and the relative value of different approaches to draining the pleural space. Image-guided small-bore catheter drainage receives special emphasis because of the unique value it provides for patients with both nonloculated and complex multiloculated infected pleural effusions.

Pathophysiologic Classification and Clinical Staging of Pleural Infections

Pleural effusions develop when the balance of pleural fluid formation and removal is altered. Pleural effusions secondary to pneumonia are termed *parapneumonic effusions*. Most of these effusions remain sterile and resolve with antibiotic therapy (termed *uncomplicated parapneumonic effusions*), but infections of the pleural space develop in a small subset of patients and require drainage for full recovery (termed *complicated parapneumonic effusions*). Without effective drainage, complicated parapneumonic effusions progress to frank intrapleural pus, which defines the presence of an empyema. This progression may occur rapidly over a few days and necessitate surgical drainage (Fig 1).

Progression to empyema occurs in three phases.[16] The exudative phase develops when inflammatory fluid enters the pleural space across vascular and visceral pleural membranes that have increased permeability due to pneumonia. Pleural fluid is nonviscous, free-flowing, and readily drained by thoracentesis or chest tube. Unremitting inflammation deposits fibrin that coats the visceral pleura and promotes the formation of locules that impede lung reexpansion during attempts at fluid drainage. Pleural fluid becomes purulent and increasingly viscous. This fibrinopurulent phase may respond to therapy with antibiotics and chest tube drainage but often requires intervention to break down adhesions. If a fibropurulent effusion remains undrained, fibroblasts eventually deposit fibrotic tissue that encases the lung in inelastic peels. At this organizing phase, resolution of the empyema requires surgical procedures to drain pus, obliterate the empyema space, and reexpand the lung.

The three phases of empyema represent a continuum of events with no clear demarcations. Biomarkers, such as pleural fluid pH, glucose, and lactate dehydrogenase, have been proposed to classify patients into a phase to guide therapy.[17] The American College of Chest Physicians (ACCP)[13] and the British Thoracic Society (BTS)[5] recommend these and other biomarkers for staging pleural infections and linking each stage with prognosis and treatment (Tables 2, 3). Because experts agree that intrapleural pus must be drained, staging systems provide value for guiding the management of nonpurulent effusions. Limited retrospective data exist[18] to establish that both the BTS and ACCP systems have high

FIGURE 1. Serial chest radiographs and CT scan images demonstrating rapid progression of infected pleural fluid to an empyema that required surgical drainage. *A*: a chest radiograph obtained at hospital admission demonstrates a right pleural effusion and parenchymal density at the right lung base. Therapy with antibiotics was begun, but thoracentesis was not performed. The effusion became massive 3 days later (*B*) when a noncontrasted CT scan (*C*) demonstrated multiple locules that contained viscous pus during surgical drainage. Without contrast, the CT scan could not clearly differentiate in some areas between loculated fluid and lung consolidation.

Table 2—ACCP System for Staging Pleural Infections and Recommending Drainage

Effusion Stage	Pleural Space Features	Bacteriology	Pleural Fluid Chemistry	Thoracentesis/Drainage
I (uncomplicated parapneumonic)	Minimal, free-flowing effusion (< 10 mm on lateral decubitus)	Culture and Gram stain results unknown	pH unknown	No/No
II (uncomplicated parapneumonic)	Small-to-moderate free-flowing effusion (> 10 mm and less than one-half hemithorax)	Negative culture and Gram stain	pH ≥ 7.20 or glucose ≥ 60 mg/dL	Yes/No
III (complicated parapneumonic)	Large, free-flowing effusion (one-half hemithorax or greater); loculated effusion; effusion with thickened parietal pleura	Positive culture or Gram stain	pH < 7.20 or glucose < 60 mg/dL	Yes/Yes
IV (empyema)		Pus	Tests not indicated	Yes/Yes

Note: Uncomplicated parapneumonic effusions left undrained should have thoracentesis repeated if the effusion enlarges or the clinical condition deteriorates. Modified from the work of Colice et al.[13]

sensitivity but only moderate specificity for identifying patients with nonpurulent effusions who require drainage.

Of note, these staging systems only apply to parapneumonic effusions. Parapneumonic effusions represent the most common cause of exudative effusions and occur in 20 to 57% of hospitalized patients with pneumonia.[17] Empyemas occur in 1 to 5% of hospitalized patients with parapneumonic effusions.[19,20] Causes of pleural infections other than pneumonia have a more complex pathophysiology. For instance, pleural infections after chest trauma develop within altered anatomic planes, and tissue hemorrhage accelerates intrapleural locules and complicates pleural fluid drainage. Staging systems provide only general roadmaps for managing infected effusions affecting patients without pneumonia (Table 1).

Therapeutic Approaches to Pleural Infections

Recommendations for managing pleural infections are limited because of the shortcomings of the evidence base. Clinical guidelines make general recommendations for managing pleural infections,[5,13] but none provides explicit suggestions for specific therapies based on the unique clinical features of the patients, underlying etiologies, and phase of empyema. Most treatment studies have observational designs. The few available randomized controlled trials enrolled small numbers of patients, aggregated diverse etiologies of empyema, did not explicitly stage pleural infections, and seldom used best practices in all study arms. Consequently, the patterns for treating individual patients typically derive from local institutional expertise and preferences and demonstrate considerable variation.

It is important, therefore, for physician groups to assess the clinical outcomes of the approaches they adopt and ensure that their outcomes match those reported in the literature. Basic principles of management (ie, rapid detection of infected pleural fluid and prompt, complete drainage when necessary) are often more important than the specific procedures used. The complexity of the conditions of these patients and the availability of advanced imaging and

Table 3—BTS Stages of Parapneumonic Effusions

Fluid Characteristics	Simple Parapneumonic Effusions	Complicated Parapneumonic Effusions	Empyema
Macroscopic appearance	Clear	Clear or cloudy/turbid	Pus
Fluid analysis			
pH	> 7.20	< 7.20	
Lactate dehydrogenase concentrations	< 1,000 IU/L	> 1,000 IU/L	
Glucose concentration	> 40 mg/dL	< 40 mg/dL	May be positive on Gram stain/culture
Gram stain	No organisms found on Gram stain or culture	May be positive on Gram stain and/or culture	
Comments	Usually resolves with antibiotics alone; perform chest tube drainage for symptom relief if required	Requires chest tube drainage	Requires chest tube drainage; no biochemical tests necessary; pH measurements not necessary

The table was modified from the work of Davies et al.[5]

therapeutic interventions warrant a multidisciplinary approach that coordinates pulmonary, thoracic surgery, and interventional radiology expertise. If pleural drainage is initiated, modifications of the treatment plan should occur based on early and frequent monitoring of the adequacy of drainage. Serial thoracenteses, blind or image-guided insertion of large-caliber or small-caliber chest tubes, intrapleural fibrinolytic therapy, thoracoscopy, and thoracotomy are the available drainage techniques. Advanced imaging studies play an important role in applying each of these modalities.

Serial Thoracentesis

When the clinical presentation and pleural fluid analysis do not establish a clear indication for pleural fluid drainage, the ACCP guidelines recommend repeating diagnostic thoracentesis to measure pleural fluid biomarkers again and reassess the need for drainage.[13] No outcome data, however, validate this approach. Some centers recommend daily therapeutic thoracentesis with or without pleural lavage when infected effusions reaccumulate after initial thoracentesis to allow patients with free-flowing fluid or single pleural locules to avoid chest tube or surgical drainage until antibiotics resolve the infection.[21–23] Serial thoracentesis also allows outpatient management.[23] This approach may require an average of eight thoracenteses in > 2 to 4 weeks.[21,22] Most experts avoid repeating multiple thoracenteses because more effective and minimally invasive drainage procedures using small-bore catheters allow faster recovery and shorter hospital stays.

Chest Tube Drainage

Insertion of a chest tube into the pleural space represents the traditional approach to draining infected pleural fluid. Chest tubes vary in size but can be classified as large-bore (> 24F to 34F) or small-bore (8F to 24F). They can be inserted without imaging guidance by a "blind" technique that directs the tube toward dependent regions of pleural fluid.[24] Alternatively, tubes can be guided by fluoroscopy, ultrasonography (US), or CT imaging.[25–27] Techniques for the insertion of chest tubes include intercostal incisions (for large-bore tubes) or use of a trocar or Seldinger technique (8F to 28F tubes). Complete reexpansion of the lung, as demonstrated by repeat imaging, resolution of clinical and laboratory signs of infection, and avoidance of surgical drainage define successful drainage.

For patients with viscous pleural pus, the surgical tradition recommends the use of large-bore chest tubes (28F to 32F) to ensure adequate drainage.[28,29] *In vitro* studies[30] support this recommendation by demonstrating lower flow rates of viscous secretions through smaller bore tubes. Multiple uncontrolled clinical studies, however, indicate that small-bore pigtail catheters (< 12F) can successfully drain infected pleural fluid, including loculated empyemas, in 70% to 100% of instances (Fig 2).[24,25,31–42] Keeling et al[31] observed similar dwell times for patients treated with 8F to 12F catheters for empyema compared with noninfectious causes of pleural effusions. Six to 20% of patients treated initially with small-bore catheters eventually require surgical drainage.[25,31,43]

Several factors promote the efficacy of small-bore catheters. Most case series of successful outcomes emphasize the importance of monitoring chest tube function and flushing tubes with a saline solution several times a day.[44] Malfunctioning tubes are immediately repositioned or replaced. Many studies[37,45] augmented pleural drainage by the use of intrapleural fibrinolytic drugs (*eg*, urokinase, streptokinase, recombinant tissue plasminogen activator [rtPA]) to lyse
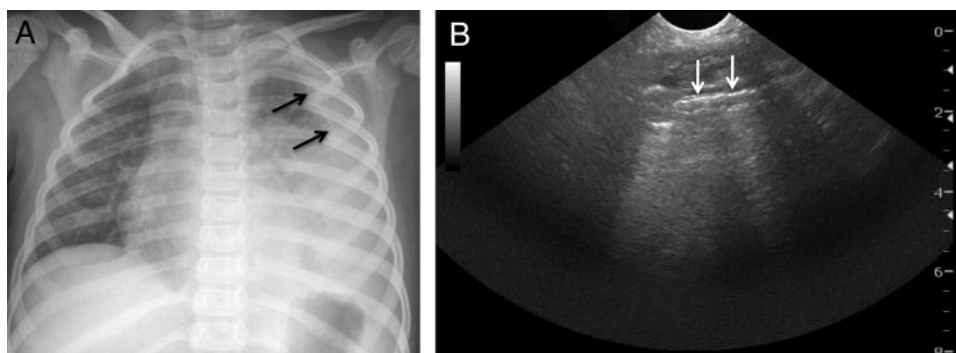

FIGURE 2. Portable chest radiograph (*A*) shows dense airspace consolidation in the left lower lobe and lingula with fluid tracking laterally (arrows). The patient underwent image-guided drainage of thick pus with a small-bore catheter. A sagittal sonographic image (*B*, cephalad to the left of the image) shows no residual fluid. The sonogram (*B*) demonstrates the echogenic visceral pleural line peripherally (arrows).
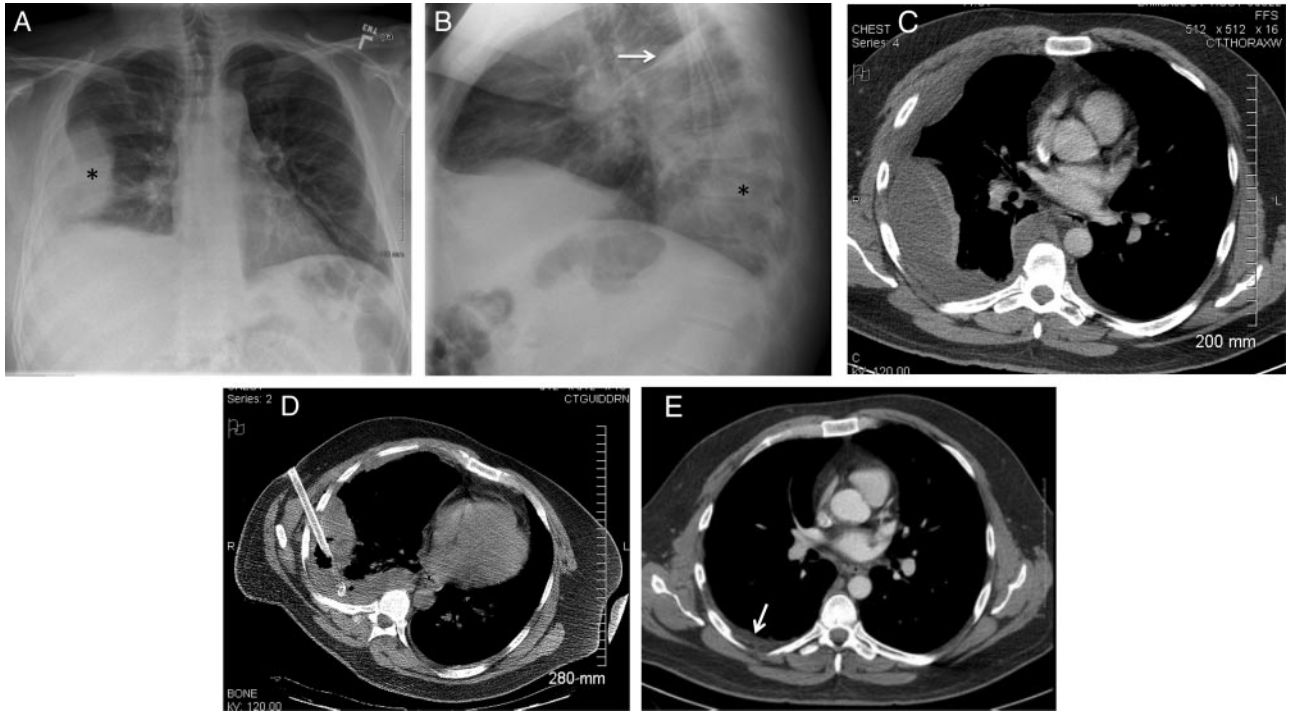
FIGURE 3. A frontal chest radiograph (*A*) and a lateral chest radiograph (*B*) show a lenticularly shaped right posterolateral pleura-based opacity (*) with a small density in the upper major fissure (arrow in *B*). Both densities were demonstrated by CT scanning to be intrapleural locules. The apparent elevation of the right diaphragm suggests a subpulmonic effusion. A contrast-enhanced CT scan through the lower chest (*C*) shows a multiloculated right pleural collection. A CT scan obtained during the placement of a 28F drainage tube (*D*) shows a tube positioned within the dependent region of the fluid collection. The patient recovered without additional interventions and had minimal residual pleural thickening 19 days later (*E*).

fibrin adhesions (see next section). Most reports[31] emphasize the importance of replacing 8F to 12F catheters with larger bore tubes (upsizing) if initial fluid drainage appears to be incomplete. Interventional radiologists can insert catheters up to 28F by image-guided trocar or Seldinger techniques (Fig 3).

Most reports[25,31,33–36,38,40,45] of the successful use of small-bore catheters recommend image guidance to ensure the placement of catheters in the most dependent fluid regions. Although one report[37] inserted initial small-bore catheters without image guidance, subsequent catheters were directed by imaging if residual fluid remained undrained. Image guidance allows placement of several catheters for multiple noncommunicating pleural fluid collections[36] including associated extrathoracic abscesses (Fig 4). Some cen-
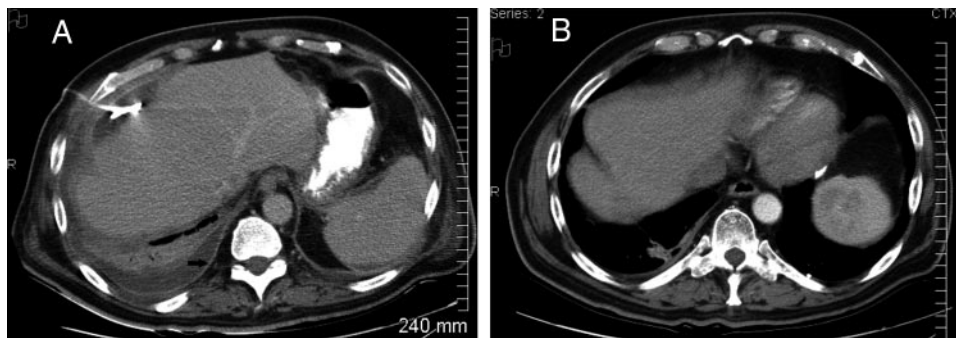

FIGURE 4. A patient with pleural empyema complicating a subcapsular hepatic abscess. A delayed postcontrast CT scan (*A*) demonstrates the posterior empyema with associated passive atelectasis of the right lung base and parietal pleural thickening (black arrow) visible. Image-guided catheters were placed for the anterior hepatic abscess and associated posterior empyema (catheter not shown), which resulted in complete resolution with minimal residual pleural thickening and parenchymal scarring seen on a CT scan image (*B*) 5 months later.

ters augment tube drainage with serial image-guided thoracentesis of residual fluid or noncommunicating locules.[45] Imaging can be performed before chest catheter insertion,[45] although most centers perform real-time imaging with CT scanning or US (Fig 5) and monitor drainage effectiveness with repeat studies. Complications occur in 3% of patients treated with image-guided small-bore catheters.[25,31,43,46] Pigtail catheter dislodgement rates are 8 to 13%.[31,43]

Because of the absence of prospective randomized trials comparing tubes of different sizes, some experts recommend[5,29,47] initial drainage by large-bore tubes. Tubes as large as 28F, however, can be placed by CT scan-guided or US-guided percutaneous techniques, and image guidance appears to be the most important factor for successful drainage. Blind tube insertion has moderate success ($< 50\%$) even with the placement of large-bore tubes.[22,39,48] Solaini et al[49] reported a lower success rate of 12% for unguided large-bore tubes for patients with ACCP stage 3 or 4 pleural infections. Failure is attributed to the misplacement of tubes distant from pleural locules, multiple noncommunicating locules, tube kinking, or obstruction by secretions. Complications, which include hemorrhage; perforation of the diaphragm, lung, or abdominal viscera; and tube misplacement into fissures or extrapleural tissue planes, develop in up to 20% of patients undergoing blind chest tube insertion.[43] Blind chest tube insertion is now reserved for patients with large, free-flowing effusions at institutions that lack the resources for image-guided drainage.

Fibrinolytic Therapy

When an infected pleural space progresses to the fibrinopurulent phase, fibrin creates intrapleural locules that impede chest tube drainage. Intrapleural instillation of fibrinolytic drugs offers a theoretical benefit for lysing fibrin adhesions, promoting pleural drainage, and avoiding surgery. Small studies have reported the beneficial effects of therapy with streptokinase, urokinase, and rtPA for avoiding surgery,[50] promoting catheter drainage,[51] and improving the radiographic appearance[45,52] of loculated effusions. Based on early reports of efficacy, the BTS[5,53] and the ACCP guidelines[13] recommend fibrinolytic drugs as management options.

Most positive studies of fibrinolytic therapy, however, have retrospective, uncontrolled designs or randomized designs with small sample sizes. In 2005, Maskell et al[20] published the findings of the Multicenter Intrapleural Sepsis Trial (MIST1), which remains the largest randomized controlled trial of fibrinolytic therapy. Study centers placed small-bore chest tubes (median size, 12F) without image guidance in 427 patients with complicated parapneumonic effusions (pleural fluid pH < 7.20, with signs of infection, or positive findings from a pleural fluid Gram stain or culture) or frank empyema and instilled streptokinase or placebo. The trial noted no benefits from streptokinase administration in terms of survival, decreased hospital stay, or need for surgery.

The MIST1 study design, however, limited its generalizability.[54] Patients did not undergo CT scanning or US imaging to identify locules or place chest tubes, and correct tube positioning was not confirmed after placement. Standardized protocols were not used to direct antibiotic or other treatments or to select patients who had not responded to fibrinolysis for surgery, which was a major end point. Streptokinase was mailed to study centers after randomization, which delayed fibrinolysis. Streptokinase was instilled routinely in all patients regardless of the adequacy of the initial chest drainage. Because most patients with parapneumonic effusions do not have loculated effusions, the overuse of fibrinolytic therapy may have obscured any efficacy achieved in subsets of patients with loculated effusions. Also, streptokinase often loses effectiveness due to immune-mediated neutralization.

Some centers now use rtPA for fibrinolysis. Walker et al[55] first reported the apparent benefits of rtPA in a patient with empyema. Subsequently, Skeete et al[56] instilled rtPA through surgical chest tubes into 42 patients with a variety of pleural conditions, of which 12 were empyemas. They reported accelerated radiographic improvement and clinical benefit. Levinson and Pennington[37] used fibrinolytic therapy for 30 patients with largely multiloculated pleural infections; 20 patients received rtPA through small-bore, image-guided chest tubes. The mean length of hospital stay was 11 days, and no
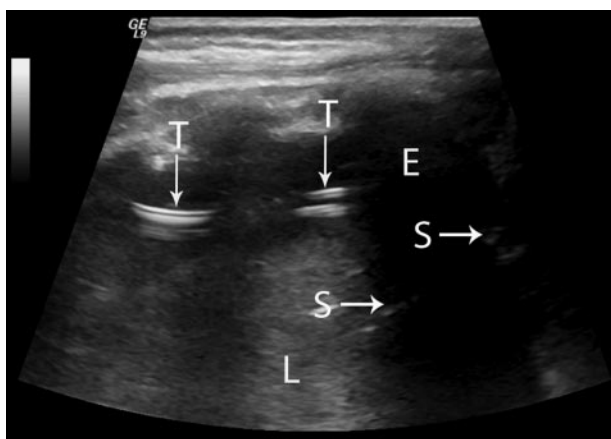

FIGURE 5. Pleural imaging (superior to left of image) during sonographically guided tube (T) drainage of an empyema (E) with multiple septations (S). L = lung.

patient required surgical drainage. Gervais et al[45] reported their experience with rtPA instilled through image-guided 8.5F to 16F catheters in 66 patients, of whom 53 had empyemas or complicated parapneumonic effusions. In the study by Gervais et al,[45] patients were selected for fibrinolysis if the initial pleural fluid drainage was incomplete. The overall success rate was 86%, although the outcomes were not specifically reported for the 53 patients with pleural infections. Based on CT imaging studies obtained before chest tube insertion that demonstrated multiple locules, the authors opined that rtPA successfully drained effusions that would otherwise have required surgery.

Since the publication of the MIST1 findings, two metaanalyses[57,58] appraised the evidence for fibrinolytic therapy and drew similar conclusions. The current evidence does not support routine fibrinolytic therapy for unselected patients with parapneumonic effusions. Because of the significant heterogeneity of the treatment effects among the trials, however, subgroups of patients with loculated or septated infected pleural effusions may benefit. As a prudent approach, pending future clinical trials would reserve therapy with fibrinolytic drugs for patients whose pleural effusions fail to drain completely after initial catheter insertion. Chest tubes should be sized appropriately for the fluid viscosity, with timely catheter upsizing performed as needed (Fig 6). Definitive surgical drainage should not be delayed for appropriate operative candidates if fibrinolysis fails to drain the effusion rapidly and completely.[59]

The viscosity of pus is largely attributable to its deoxyribose nucleoprotein content. Fibrinolytic drugs have negligible effects on decreasing the viscosity of empyema pus in contrast to agents that depolymerize DNA, such as human recombinant deoxyribonuclease.[60] Recombinant deoxyribonuclease has been reported[61] to improve drainage in a single patient who did not respond to fibrinolytic therapy.

The complications of fibrinolysis include chest pain, fever, hemothorax, hematuria, and allergic reactions to streptokinase (Fig 7).[20,56] With the use of rtPA, systemic hemorrhage has not been reported except in patients receiving concomitant full-dose anticoagulation.[45] A Cochrane review[58] reported that intrapleural fibrinolytic therapy has not been shown to increase the number of adverse events resulting from chest tube drainage, but the confidence interval around this observation is too wide to firmly exclude this possibility.

Thoracoscopy

Thoracoscopy provides minimally invasive access to the pleural space for patients with free-flowing or multiloculated effusions to suction viscous pleural fluid, lyse adhesions to promote drainage of locules, and place chest tubes in dependent regions of pleural fluid under direct visualization. Visual inspection of the pleural space after debridement determines whether patients should be converted to therapy with decortication by thoracotomy; the inability of the reinflated lung to expand to the chest wall and diaphragm indicates an unsuccessful thoracoscopy and a need for thoracotomy.[62] The advantages of thoracoscopic pleural drainage compared with thoracotomy include less postoperative pain, lower costs, shorter hospital stays, and better cosmetic results. Available thoracoscopic procedures include medical thoracoscopy and video-assisted thoracoscopic surgery (VATS).

Medical thoracoscopy can drain some established empyemas.[63,64] Pulmonary physicians or surgeons can perform the procedure in endoscopy suites using local anesthetics and moderate sedation. US identifies an entry site for the thoracoscope where the effusion is the largest and most distant from the diaphragm.[28] The advantages of medical thoracoscopy compared with VATS include lower cost and
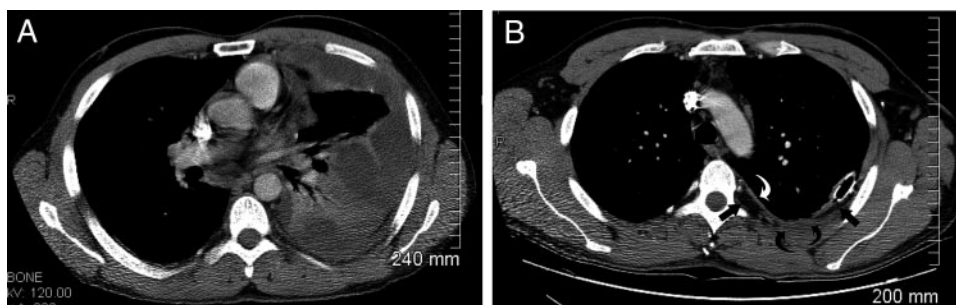

FIGURE 6. Chest CT scan image of a multiloculated empyema (*A*) that required percutaneous placement of a large-bore catheter. After subsequent instillation of rtPA, a contrast-enhanced scan (*B*) at the level of the aortic arch shows the tube in the pleural space posteriorly with minimal residual pleural fluid or thickening (white curved arrows) and regions of edema (black curved arrows) of the extrapleural fat (black straight arrows), a finding often seen on CT scans of patients with empyema.
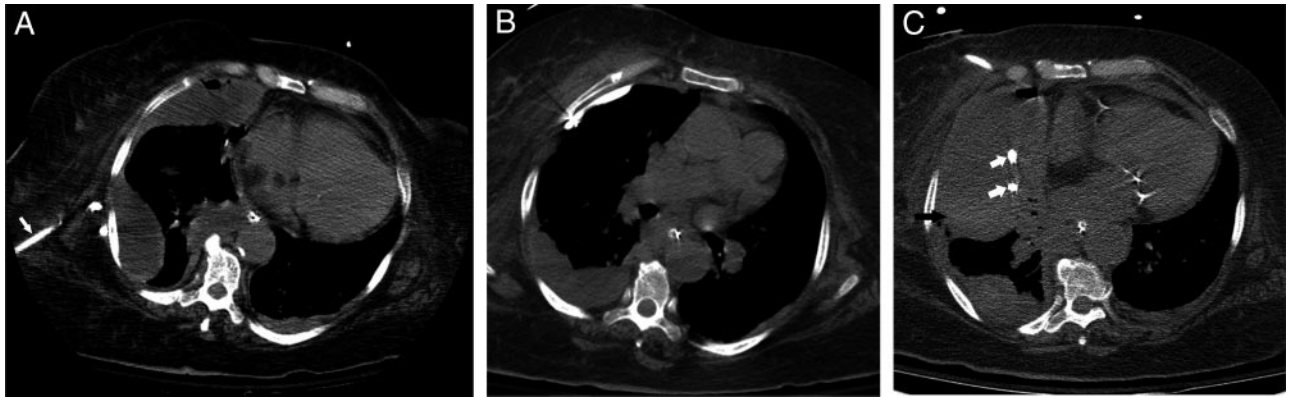
FIGURE 7. Hemothorax complicating intrapleural instillation of rtPA for a loculated empyema. An unenhanced CT scan (*A*) shows right anterior, posterolateral, and paraspinal and small left pleural fluid collections with a pigtail catheter entering the right chest wall (arrow) with its tip terminating in the posterolateral fluid collection (not shown in *A*). Intrapleural rtPA was instilled into the anterior fluid collection through a second pigtail catheter. Three days later (*B*), the anterior collection drained but posterolateral collection persisted. After the instillation of additional rtPA, pleural drainage became bloody, and a repeat unenhanced CT scan (*C*) demonstrated a large, anterior fluid collection with high-attenuation material dependently (black arrow) reflecting a loculated hemothorax that displaced the anterior catheter (white arrows). The posterior fluid collection in *C* increased slightly compared with *B*, suggesting posterior accumulation of blood from the anterior hemorrhage. This series of images demonstrates the difficulty in establishing by CT scan whether different pleural fluid collections intercommunicate.

better tolerance by frail patients who may not tolerate lung deflation, which is required for VATS.[65,66] For carefully selected patients with fibrinopurulent pleural infections and locules within reach of the thoracoscope, medical thoracoscopy has a reported success rate of 93% with a small proportion of patients needing conversion to VATS or open surgical drainage.[28]

A thoracic surgeon performs VATS with patients under general anesthesia using a three-entry port and a double-lumen endotracheal tube, although local or regional anesthesia and two-port approaches have been reported.[67] Decortication and pleurectomy can be performed. VATS provides wide access to the pleural space in many patients but may be inadequate to reach all fluid collections for advanced empyemas and dense adhesions or widely distributed locules.[62] The overall success rate, as defined by complete recovery without requiring thoracotomy, is 60 to 100% for fibrinopurulent effusions.[68–71] Many centers reserve VATS for the treatment of patients with fibrinopurulent effusions,[72] although some surgeons initially treat empyemas in the organizing phase with VATS, with conversion to thoracotomy if necessary.[62,73–75] Roberts[62] has supported this approach by emphasizing that preoperative evaluations cannot establish with certainty the phase of a pleural space infection, which requires assessment under direct VATS visualization. The series of patients with fibrinopurulent or organizing empyemas treated initially by VATS had a success rate of 38% and a hospital mortality rate of 6.6%. All of the deaths occurred in those patients who did not respond to treatment with VATS and who then required thoracotomy.

No large randomized studies directly compare the utility of chest tube drainage with or without fibrinolytic therapy vs thoracoscopy.[68] A small, randomized trial[76] compared chest tube drainage plus fibrinolytic therapy with VATS and found shorter hospitalizations with VATS. This study was limited by its small size and methodological problems.[77] Another randomized trial[78] of 70 patients compared treatment with VATS with chest tube drainage without fibrinolytic therapy and observed shorter hospitalizations and less need for open decortication after primary treatment with VATS. Chest tubes were placed without image guidance, however, and the clinicians who made the treatment decisions were not blinded. Epidemiologic data from the state of Washington[9] noted a lower overall mortality for patients with empyema from 1987 to 2004, during which time progressively more patients underwent surgical drainage (either thoracotomy or thoracoscopy), as opposed to chest tube drainage. Patients treated with chest tube drainage, however, most likely underwent standard incisional chest tube insertion without image guidance. Modern protocols calling for the early use of small-bore, image-guided catheters may compare more favorably with VATS in future trials.

In the absence of data from adequate trials, the decision to proceed directly to thoracoscopy vs an initial trial of chest tube drainage remains ill defined.[49] Some experts[79,80] have proposed initial thoracoscopy for all patients with fibrinopurulent or organized empyemas, while others[81] have recommended a trial of image-guided catheter drainage with or without fibrinolytic therapy. Regardless of the approach, definitive surgical drainage should not be delayed inappropriately if initial drainage by chest
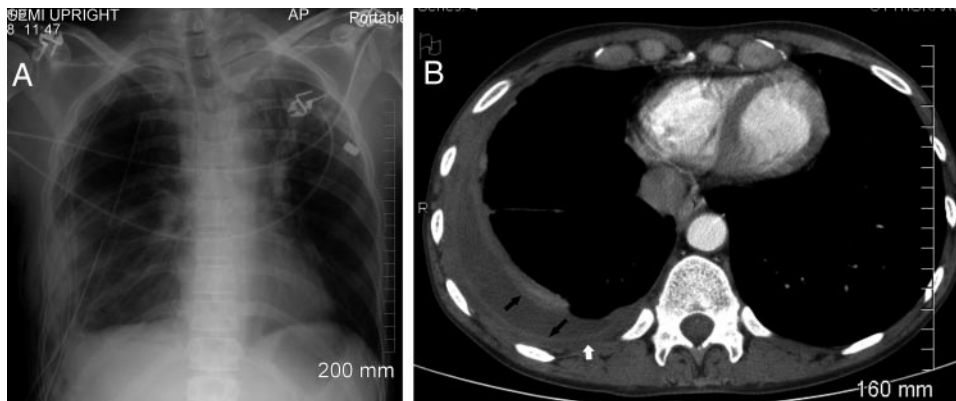
FIGURE 8. A patient with a right-sided empyema underwent VATS because fluid was loculated and could not be sampled by diagnostic thoracentesis. The postoperative chest radiograph (*A*) demonstrated large-bore chest tubes, and left upper lobe fibronodular densities and apical pleural capping consistent with the previously treated tuberculosis of the patient. A postoperative CT scan (*B*) demonstrated residual fluid, which drained subsequently through the superiorly placed chest tubes (not shown in *B*). The CT scan (*B*) demonstrates the split pleura sign with separation of the contrast-enhanced visceral and parietal pleura (black arrows), which suggests intrapleural infection. The CT scan also shows expansion of the extrapleural fat (white arrow).

tubes proves unsuccessful.[81] Experts variably define the acceptable durations of catheter trials before thoracoscopy as 1 to 7 days.[5,29,36,53,59,79] The disadvantages of delaying thoracoscopy for a catheter trial are ill defined. One study observed that primary therapy with VATS for the drainage of complicated parapneumonic effusions had a higher success rate compared with secondary VATS after a failed trial of catheter drainage with fibrinolysis.[82] The viewpoints of the patients regarding the risks and benefits of attempting chest tube drainage in an effort to avoid surgery should enter into decision making. In our experience, the failure to aspirate pleural fluid through an initial image-guided thoracentesis warrants immediate referral to VATS (Fig 8).

Thoracotomy, Decortication, and Open Drainage

Complete or partial decortication through a full or limited thoracotomy can evacuate intrapleural pus and remove fibrous tissue that coats the visceral and parietal pleura and prevents lung reexpansion.[83] Thoracotomy remains the main salvage procedure after unsuccessful thoracoscopy, as defined by the failure of lung expansion to the chest wall.[62,72,84] Performed in appropriate operative candidates, the
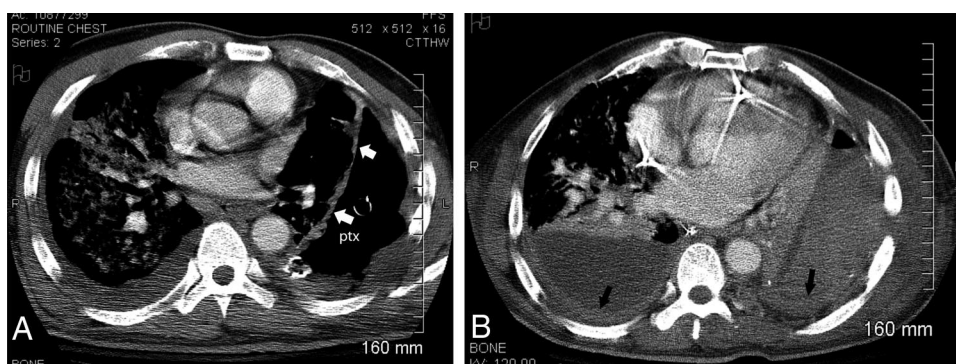

FIGURE 9. A patient with a chronic left-sided empyema and bronchopleural fistula due to recurrent pneumonia underwent drainage of pleural pus with a large-bore chest tube. The initial chest CT scan (*A*) also shows middle and right lower lobe airspace opacities and a chronic right effusion that was not infected at the time. There is left visceral pleural thickening (arrows) with a left pneumothorax (ptx) and lobulated parietal pleural thickening. Several months after removal of the chest tube, another CT scan (*B*) showed a high-density, left-sided pleural fluid with no reexpansion of the left lung and a thick parietal pleura (arrow). The right effusion has increased in size with passive right lower lobe atelectasis, with associated parietal pleural thickening (arrow) due to intrapleural infection. The patient underwent open drainage of the left effusion and placement of a right intrapleural catheter.

mortality rate is 3% to 10%[85,86] with a median postsurgery hospital stay of 7 days.[85] Patients with organized empyemas who cannot tolerate thoracotomy or have trapped lungs can undergo rib resection with open drainage. Pus drains through a chest wound placed for ≥ 6 months.[5,87–89] Chronic empyemas with bronchopleural fistulas also may require long-term open drainage to prevent persistent pleural suppuration when patients are treated with chest tube drainage alone (Fig 9). Recently, the use of an image-guided, small-bore catheter has been described[90] for the long-term drainage of chronic empyemas that are not amenable to surgery.

Decortication by thoracotomy is also indicated for seriously ill and toxic patients with associated mediastinitis or bronchopleural fistulas who require mediastinal drainage or fistula closure.[72] Also, some experts[72] recommend proceeding directly to thoracotomy (or VATS in selected instances) without prior chest tube drainage for toxic patients with virulent multi-drug-resistant pathogens and multiorgan dysfunction, who have a high mortality rate and may benefit from immediate drainage.

Conclusion

Modern principles of managing pleural space infections emphasize the importance of the early detection of effusions in patients with pneumonia, and the prompt drainage of complicated parapneumonic effusions and empyemas. Delays in effective drainage increase morbidity and mortality. As outlined in this review, multiple interventions exist to detect and drain pleural fluid with limited data from rigorous clinical trials to establish the superiority of any single approach. Clinicians should establish standardized protocols in their institutions for early identification and management based on available expertise and resources. Regardless of the approach adopted, measured outcomes should match the best practices reported in the literature.

Acknowledgments

References

1 Ferguson AD, Prescott RJ, Selkon JB, et al. The clinical course and management of thoracic empyema. QJM 1996; 89:285–289
2 Davies CWH, Kearney SE, Gleeson FV, et al. Predictors of outcome and long-term survival in patients with pleural infection. Am J Respir Crit Care Med 1999; 160:1682–1687
3 Ashbaugh DG. Empyema thoracis: factors influencing morbidity and mortality. Chest 1991; 99:1162–1165
4 Bouros D, Schiza S, Patsourakis G, et al. Intrapleural streptokinase versus urokinase in the treatment of complicated parapneumonic effusions: a prospective, double-blind study. Am J Respir Crit Care Med 1997; 155:291–295
5 Davies CW, Gleeson FV, Davies RJ. BTS guidelines for the management of pleural infection. Thorax 2003; 58(suppl): ii18–ii28
6 Mandal AK, Thadepalli H, Mandal AK, et al. Outcome of primary empyema thoracis: therapeutic and microbiologic aspects. Ann Thorac Surg 1998; 66:1782–1786
7 Smith JA, Mullerworth MH, Westlake GW, et al. Empyema thoracis: 14-year experience in a teaching center. Ann Thorac Surg 1991; 51:39–42
8 Tsai TH, Jerng JS, Chen KY, et al. Community-acquired thoracic empyema in older people. J Am Geriatr Soc 2005; 53:1203–1209
9 Farjah F, Symons RG, Krishnadasan B, et al. Management of pleural space infections: a population-based analysis. J Thorac Cardiovasc Surg 2007; 133:346–351
10 Finley C, Clifton J, Fitzgerald JM, et al. Empyema: an increasing concern in Canada. Can Respir J 2008; 15:85–89
11 Lin YC, Tu CY, Chen W, et al. An urgent problem of aerobic gram-negative pathogen infection in complicated parapneumonic effusions or empyemas. Intern Med 2007; 46:1173–1178
12 Foster S, Maskell N. Bacteriology of complicated parapneumonic effusions. Curr Opin Pulm Med 2007; 13:319–323
13 Colice GL, Curtis A, Deslauriers J, et al. Medical and surgical treatment of parapneumonic effusions: an evidence-based guideline. Chest 2000; 118:1158–1171
14 Heffner JE, McDonald J, Barbieri C, et al. Management of parapneumonic effusions: an analysis of physician practice patterns. Arch Surg 1995; 130:433–438
15 Chu MW, Dewar LR, Burgess JJ, et al. Empyema thoracis: lack of awareness results in a prolonged clinical course. Can J Surg 2001; 44:284–288
16 Andrews NC, Parker EF, Shaw RR, et al. Management of nontruberculous empyema. Am Rev Respir Dis 1962; 85: 935–936
17 Light RW. Parapneumonic effusions and empyema. Proc Am Thorac Soc 2006; 3:75–80
18 Manuel Porcel J, Vives M, Esquerda A, et al. Usefulness of the British Thoracic Society and the American College of Chest Physicians guidelines in predicting pleural drainage of non-purulent parapneumonic effusions. Respir Med 2006; 100:933–937
19 Ahmed RA, Marrie TJ, Huang JQ. Thoracic empyema in patients with community-acquired pneumonia. Am J Med 2006; 119:877–883
20 Maskell NA, Davies CW, Nunn AJ, et al. UK Controlled trial of intrapleural streptokinase for pleural infection. N Engl J Med 2005; 352:865–874
21 Simmers TA, Jie C, Sie B. Minimally invasive treatment of thoracic empyema. Thorac Cardiovasc Surg 1999; 47:77–81
22 Storm HK, Krasnik M, Bang K, et al. Treatment of pleural empyema secondary to pneumonia: thoracocentesis regimen versus tube drainage. Thorax 1992; 47:821–824
23 Sasse S, Nguyen T, Teixeira LR, et al. The utility of daily therapeutic thoracentesis for the treatment of early empyema. Chest 1999; 116:1703–1708
24 Stavas J, vanSonnenberg E, Casola G, et al. Percutaneous drainage of infected and noninfected thoracic fluid collections. J Thorac Imaging 1987; 2:80–87

25 Moulton JS, Benkert RE, Weisiger KH, et al. Treatment of complicated pleural fluid collections with image-guided drainage and intracavitary urokinase. Chest 1995; 108:1252–1259

26 Klein JS, Schultz S, Heffner JE. Interventional radiology of the chest: Image-guided percutaneous drainage of pleural effusions, lung abscess, and pneumothorax. Am J Roentgenol 1995; 164:581–588

27 Rosenberg ER. Ultrasound in the assessment of pleural densities. Chest 1983; 84:283–285

28 Tassi GF, Davies RJ, Noppen M. Advanced techniques in medical thoracoscopy. Eur Respir J 2006; 28:1051–1059

29 Yim AP. Paradigm shift in empyema management. Chest 1999; 115:611–612

30 Park JK, Kraus FC, Haaga JR. Fluid flow during percutaneous drainage procedures: an *in vitro* study of the effects of fluid viscosity, catheter size, and adjunctive urokinase. Am J Roentgenol 1993; 160:165–169

31 Keeling AN, Leong S, Logan PM, et al. Empyema and effusion: outcome of image-guided small-bore catheter drainage. Cardiovasc Intervent Radiol 2008; 31:135–141

32 Liang SJ, Chen W, Lin YC, et al. Community-acquired thoracic empyema in young adults. South Med J 2007; 100:1075–1080

33 Ulmer JL, Choplin RH, Reed JC. Image-guided catheter drainage of the infected pleural space. J Thorac Imaging 1991; 6:65–73

34 Westcott JL. Percutaneous catheter drainage of pleural effusion and empyema. Am J Roentgenol 1985; 144:1189–1193

35 Merriam MA, Cronan JJ, Dorfman GS, et al. Radiographically guided percutaneous catheter drainage of pleural fluid collections. Am J Roentgenol 1988; 151:1113–1116

36 Akhan O, Ozkan O, Akinci D, et al. Image-guided catheter drainage of infected pleural effusions. Diagn Interv Radiol 2007; 13:204–209

37 Levinson GM, Pennington DW. Intrapleural fibrinolytics combined with image-guided chest tube drainage for pleural infection. Mayo Clin Proc 2007; 82:407–413

38 Shankar S, Gulati M, Kang M, et al. Image-guided percutaneous drainage of thoracic empyema: can sonography predict the outcome? Eur Radiol 2000; 10:495–499

39 Moulton JS. Image-guided management of complicated pleural fluid collections. Radiol Clin North Am 2000; 38:345–374

40 Moulton JS, Moore PT, Mencini RA. Treatment of loculated pleural effusions with transcatheter intracavitary urokinase. Am J Roentgenol 1989; 153:941–945

41 vanSonnenberg E, Nakamoto SK, Mueller PR, et al. CT- and ultrasound-guided catheter drainage of empyemas after chest-tube failure. Radiology 1984; 151:349–353

42 Silverman SG, Mueller PR, Saini S, et al. Thoracic empyema: management with image-guided catheter drainage. Radiology 1988; 169:5–9

43 Horsley A, Jones L, White J, et al. Efficacy and complications of small-bore, wire-guided chest drains. Chest 2006; 130: 1857–1863

44 Cheng G, Vintch JR. A retrospective analysis of the management of parapneumonic empyemas in a county teaching facility from 1992 to 2004. Chest 2005; 128:3284–3290

45 Gervais DA, Levis DA, Hahn PF, et al. Adjunctive intrapleural tissue plasminogen activator administered via chest tubes placed with imaging guidance: effectiveness and risk for hemorrhage. Radiology 2008; 246:956–963

46 Parulekar W, Di Primio G, Matzinger F, et al. Use of small-bore vs large-bore chest tubes for treatment of malignant pleural effusions. Chest 2001; 120:19–25

47 Hyde J, Sykes T, Graham T. Reducing morbidity from chest drains. BMJ 1997; 314:914–915

48 Ali I, Unruh H. Management of empyema thoracis. Ann Thorac Surg 1990; 50:355–359

49 Solaini L, Prusciano F, Bagioni P. Video-assisted thoracic surgery in the treatment of pleural empyema. Surg Endosc 2007; 21:280–284

50 Diacon AH, Theron J, Schuurmans MM, et al. Intrapleural streptokinase for empyema and complicated parapneumonic effusions. Am J Respir Crit Care Med 2004; 170:49–53

51 Bouros D, Schiza S, Tzanakis N, et al. Intrapleural urokinase versus normal saline in the treatment of complicated parapneumonic effusions and empyema: a randomized, double-blind study. Am J Respir Crit Care Med 1999; 159:37–42

52 Davies RJO, Traill ZC, Gleeson FV. Randomised controlled trial of intrapleural streptokinase in community acquired pleural infection. Thorax 1997; 52:416–421

53 Balfour-Lynn IM, Abrahamson E, Cohen G, et al. BTS guidelines for the management of pleural infection in children. Thorax 2005; 60(suppl):i1–i21

54 Heffner JE. Multicenter trials of treatment for empyema: after all these years. N Engl J Med 2005; 352:926–928

55 Walker CA, Shirk MB, Tschampel MM, et al. Intrapleural alteplase in a patient with complicated pleural effusion. Ann Pharmacother 2003; 37:376–379

56 Skeete DA, Rutherford EJ, Schlidt SA, et al. Intrapleural tissue plasminogen activator for complicated pleural effusions. J Trauma 2004; 57:1178–1183

57 Tokuda Y, Matsushima D, Stein GH, et al. Intrapleural fibrinolytic agents for empyema and complicated parapneumonic effusions: a meta-analysis. Chest 2006; 129:783–790

58 Cameron R, Davies HR. Intra-pleural fibrinolytic therapy versus conservative management in the treatment of adult parapneumonic effusions and empyema. Cochrane Database Syst Rev (database online). Issue 1, 2008

59 Bouros D, Tzouvelekis A, Antoniou KM, et al. Intrapleural fibrinolytic therapy for pleural infection. Pulm Pharmacol Ther 2007; 20:616–626

60 Simpson G, Roomes D, Heron M. Effects of streptokinase and deoxyribonuclease on viscosity of human surgical and empyema pus. Chest 2000; 117:1728–1733

61 Simpson G, Roomes D, Reeves B. Successful treatment of empyema thoracis with human recombinant deoxyribonuclease. Thorax 2003; 58:365–366

62 Roberts JR. Minimally invasive surgery in the treatment of empyema: intraoperative decision making. Ann Thorac Surg 2003; 76:225–230

63 Loddenkemper R, Boutin C. Thoracoscopy: present diagnostic and therapeutic indications. Eur Respir J 1993; 6:1544–1555

64 Mathur PN, Loddenkemper R. Medical thoracoscopy: role in pleural and lung diseases. Clin Chest Med 1995; 16:487–496

65 Colt HG. Thoracoscopy: a prospective study of safety and outcome. Chest 1995; 108:324–329

66 Soler M, Wyser C, Bolliger CT, et al. Treatment of early parapneumonic empyema by "medical" thoracoscopy. Schweiz Med Wochenschr 1997; 127:1748–1753

67 Drain AJ, Ferguson JI, Sayeed R, et al. Definitive management of advanced empyema by two-window video-assisted surgery. Asian Cardiovasc Thorac Ann 2007; 15:238–239

68 Waller DA. Thoracoscopy in management of postpneumonic pleural infections. Curr Opin Pulm Med 2002; 8:323–326

69 Cassina PC, Hauser M, Hillejan L, et al. Video-assisted thoracoscopy in the treatment of pleural empyema: stage-based management and outcome. J Thorac Cardiovasc Surg 1999; 117:234–238

70 Sasse SA. Parapneumonic effusions and empyema. Curr Opin Pulm Med 1996; 2:320–326

71 Silen ML, Naunheim KS. Thoracoscopic approach to the

management of empyema thoracis: indications and results. Chest Surg Clin N Am 1996; 6:491–499

72 Potaris K, Mihos P, Gakidis I, et al. Video-thoracoscopic and open surgical management of thoracic empyema. Surg Infect 2007; 8:511–517

73 Lackner RP, Hughes R, Anderson LA, et al. Video-assisted evacuation of empyema is the preferred procedure for management of pleural space infections. Am J Surg 2000; 179:27–30

74 Suzuki T, Kitami A, Suzuki S, et al. Video-assisted thoracoscopic sterilization for exacerbation of chronic empyema thoracis. Chest 2001; 119:277–280

75 Waller DA, Rengarajan A. Thoracoscopic decortication: a role for video-assisted surgery in chronic postpneumonic pleural empyema. Ann Thorac Surg 2001; 71:1813–1816

76 Wait MA, Sharma S, Hohn J, et al. A randomized trial of empyema therapy. Chest 1997; 111:1548–1551

77 Coote N, Kay E. Surgical versus non-surgical management of pleural empyema. Cochrane Database Syst Rev (databse online). Issue 3, 2005

78 Bilgin M, Akcali Y, Oguzkaya F. Benefits of early aggressive management of empyema thoracis. ANZ J Surg 2006; 76: 120–122

79 Brutsche MH, Tassi GF, Gyorik S, et al. Treatment of sonographically stratified multiloculated thoracic empyema by medical thoracoscopy. Chest 2005; 128:3303–3309

80 Sendt W, Forster E, Hau T. Early thoracoscopic debridement and drainage as definite treatment for pleural empyema. Eur J Surg 1995; 161:73–76

81 Lim TK, Chin NK. Empirical treatment with fibrinolysis and early surgery reduces the duration of hospitalization in pleural sepsis. Eur Respir J 1999; 13:514–518

82 Petrakis IE, Kogerakis NE, Drositis IE, et al. Video-assisted thoracoscopic surgery for thoracic empyema: primarily, or after fibrinolytic therapy failure? Am J Surg 2004; 187:471–474

83 Thurer RJ. Decortication in thoracic empyema: indications and surgical technique. Chest Surg Clin N Am 1996; 6:461–490

84 Angelillo Mackinlay TA, Lyons GA, Chimondeguy DJ, et al. VATS debridement versus thoracotomy in the treatment of loculated postpneumonia empyema. Ann Thorac Surg 1996; 61:1626–1630

85 Pothula V, Krellenstein DJ. Early aggressive surgical management of parapneumonic empyemas. Chest 1994; 105:832–836

86 Grotenhuis BA, Janssen PJ, Eerenberg JP. The surgical treatment of stage III empyema: the effect on lung function. Minerva Chir 2008; 63:23–27

87 Deslauriers J, Jacques LF, Gregoire J. Role of Eloesser flap and thoracoplasty in the third millennium. Chest Surg Clin N Am 2002; 12:605–623

88 Athanassiadi K, Gerazounis M, Kalantzi N. Treatment of post-pneumonic empyema thoracis. Thorac Cardiovasc Surg 2003; 51:338–341

89 Thourani VH, Lancaster RT, Mansour KA, et al. Twenty-six years of experience with the modified eloesser flap. Ann Thorac Surg 2003; 76:401–406

90 Davies HE, Rahman NM, Parker RJ, et al. Use of indwelling pleural catheters for chronic pleural infection. Chest 2008; 133:546–549

Interventional Management of Pleural Infections

John E. Heffner, Jeffrey S. Klein and Christopher Hampson

This information is current as of November 2, 2009

Updated Information & Services	Updated Information and services, including high-resolution figures, can be found at: http://chestjournal.chestpubs.org/content/136/4/1148.full.html
References	This article cites 88 articles, 55 of which can be accessed free at: **http://chestjournal.chestpubs.org/content/136/4/1148.full.html#ref-list-1**
Open Access	Freely available online through CHEST open access option
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://www.chestjournal.org/site/misc/reprints.xhtml
Reprints	Information about ordering reprints can be found online: http://www.chestjournal.org/site/misc/reprints.xhtml
Email alerting service	Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.
Images in PowerPoint format	Figures that appear in CHEST articles can be downloaded for teaching purposes in PowerPoint slide format. See any online article figure for directions

AMERICAN COLLEGE OF
CHEST
PHYSICIANS®