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Parapneumonic Pleural Effusion and Empyema

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Key Words
Parapneumonic pleural effusion · Empyema · Fibrinolytics · Thoracoscopy · Thoracotomy · Thoracostomy

Abstract
At least 40% of all patients with pneumonia will have an associated pleural effusion, although a minority will require an intervention for a complicated parapneumonic effusion or empyema. All patients require medical management with antibiotics. Empyema and large or loculated effusions need to be formally drained, as well as parapneumonic effusions with a pH <7.20, glucose <3.4 mmol/l (60 mg/dl) or positive microbial stain and/or culture. Drainage is most frequently achieved with tube thoracostomy. The use of fibrinolytics remains controversial, although evidence suggests a role for the early use in complicated, loculated parapneumonic effusions and empyema, particularly in poor surgical candidates and in centres with inadequate surgical facilities. Early thoracoscopy is an alternative to thrombolytics, although its role is even less well defined than fibrinolytics. Local expertise and availability are likely to dictate the initial choice between tube thoracostomy (with or without fibrinolytics) and thoracoscopy. Open surgical intervention is sometimes required to control pleural sepsis or to restore chest mechanics. This review gives an overview of parapneumonic effusion and empyema, focusing on recent developments and controversies.

Previous articles in this series: 1. Froudarakis ME: Diagnostic work-up of pleural effusions. *Respiration* 2008;75:4–13. 2. Jantz MA, Antony VB: Pathophysiology of the pleura. *Respiration* 2008;75:121–133.

Introduction and Definitions

At least 40% of all patients diagnosed with pneumonia will have an associated pleural effusion, although the minority of these will require active intervention [1, 2]. A parapneumonic pleural effusion refers to any effusion secondary to pneumonia or lung abscess [1]. It becomes 'complicated' when an invasive procedure is necessary for its resolution, or if bacteria can be cultured from the effusion [1]. Empyema is a term derived from the Greek verb *empyein* ('to suppurate') and literally refers to frank pus in the pleural space. Parapneumonic effusion and empyema remain important medical conditions associated with significant morbidity and mortality [2]. It is estimated that in the United States alone, pleural infections have an incidence of 60,000 per year and a mortality of approximately 15% [3, 4]. Yet, controversy remains regarding the management and specifically the role of fibrinolytic therapy.

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Epidemiology and Risk Factors

Complicated parapneumonic effusions and empyema are more common at both extremes of age [2, 3]. At least two thirds of patients will have an identifiable risk factor at presentation [2], which may include immunosuppressive states (most frequently HIV infection, diabetes mellitus and malnutrition), alcohol or intravenous drug abuse, bronchial aspiration, poor dental hygiene, gastro-oesophageal reflux, and chronic parenchymal lung disease [3, 4]. Microbial virulence and idiosyncrasies of the immune system are often also implicated, principally in individuals with no apparent predisposition.

Pathogenesis

Although pleural infection may occur as a primary event, most cases of pleural sepsis are secondary to pneumonias, lung abscesses or infective exacerbations of bronchiectasis. It should be noted that the associated pulmonary consolidation may be minimal [2]. Other identifiable causes include thoracic surgery, diagnostic procedures involving the pleural space, trauma, oesophageal rupture, transdiaphragmatic spread and rarely bronchial obstruction [5]. Primary pleural infections are presumably most often due to the haematogenous spread of organisms from gingival and upper respiratory tract infections (with cultures yielding oropharyngeal flora and anaerobes) [2, 6] or due to *Mycobacterium tuberculosis* [7].

The development of a parapneumonic effusion occurs in three clinically relevant stages that represent a continuous spectrum [1, 8]. A rapid influx of exudative fluid into the pleural space is observed in up to 40% of patients with pneumonia and heralds the first or exudative stage [1, 2]. The accumulation of fluid is thought to be a direct result of increased pulmonary interstitial fluid traversing the pleura to enter the pleural space [1] and an increase in vascular permeability secondary to pro-inflammatory cytokines [2, 9], e.g. interleukin-8 and tumour necrosis factor-α. During this stage pleural fluid culture is negative for bacteria, fluid pH is >7.20, the glucose level is within the normal range and lactate dehydrogenase remains <3 times the upper limit of normal [1, 2]. Most patents with uncomplicated parapneumonic effusions will respond to antibiotics alone and drainage is generally not required [1, 2, 10].

Untreated exudative effusions may develop into fibrinopurulent effusions. This second stage is characterized by positive microbial cultures. Ongoing phagocytosis and cell lysis result in fluid that most frequently has a pH of <7.20, a lactate dehydrogenase >3 times the upper limit and a low glucose [1, 2, 10]. Rarely, fibrinopurulent effusions can have a pH in the normal or even in the alkaline range. This phenomenon is limited to a few pathogens (e.g. *Proteus* spp.) with enzymatic activity that can elevate fluid pH, for instance by cleaving urea into ammonia [11]. During the fibrinopurulent stage the pleural space becomes increasingly infected. Loculations may develop and closed or open drainage becomes necessary – the point in time where an effusion is referred to as 'complicated'. A critical characteristic of the fibrinopurulent stage of pleural sepsis is the disturbance of the physiological equilibrium between clotting and fibrinolysis within the pleural space [2, 12]. Several mediators for the activation of the coagulation cascade and inhibition of fibrinolysis have been suggested: TNF-α, for example, has been shown to stimulate the release of plasminogen activator inhibitors from pleural mesothelial cells. Aleman et al. [13] were able to show increased levels of plasminogen activator inhibitor-2 and depressed levels of tissue plasminogen activator (tPA) during complicated pleural sepsis. Although the exact mechanisms behind the procoagulate state still need to be elucidated, its effects are well-known: pleural surfaces coated with fibrin and fibrin strands with secondary adhesions and loculations, all complicating pleural fluid drainage.

The third and final stage of pleural infection is the organizing phase [1, 2]. Fibroblasts grow into the pleural space from both the visceral and parietal pleura. This eventually results in a thick pleural peel, which restricts chest mechanics and often necessitates a surgical decortication to address restrictive impairment. Recent research on animal models has suggested a cardinal role for transforming growth factor-β_1 as a fibrogenic cytokine in the development of pleural fibrosis [14].

Bacteriology

The reported bacteriology of pleural sepsis varies significantly between community-acquired and nosocomial infections [2]. Maskell et al. [15] reported the large prospective MIST 1 trial (Multicenter Intrapleural Sepsis Trial 1) in 2005. Their study included 430 subjects across 52 centres in the United Kingdom. Of these, 232 (54%) had positive pleural cultures. The *Streptococcus milleri* group was the most common pathogen (29%), followed by staphylococci (21%) and *Streptococcus pneumoniae* (16%). Anaerobes were isolated in 15%. Other isolates in-

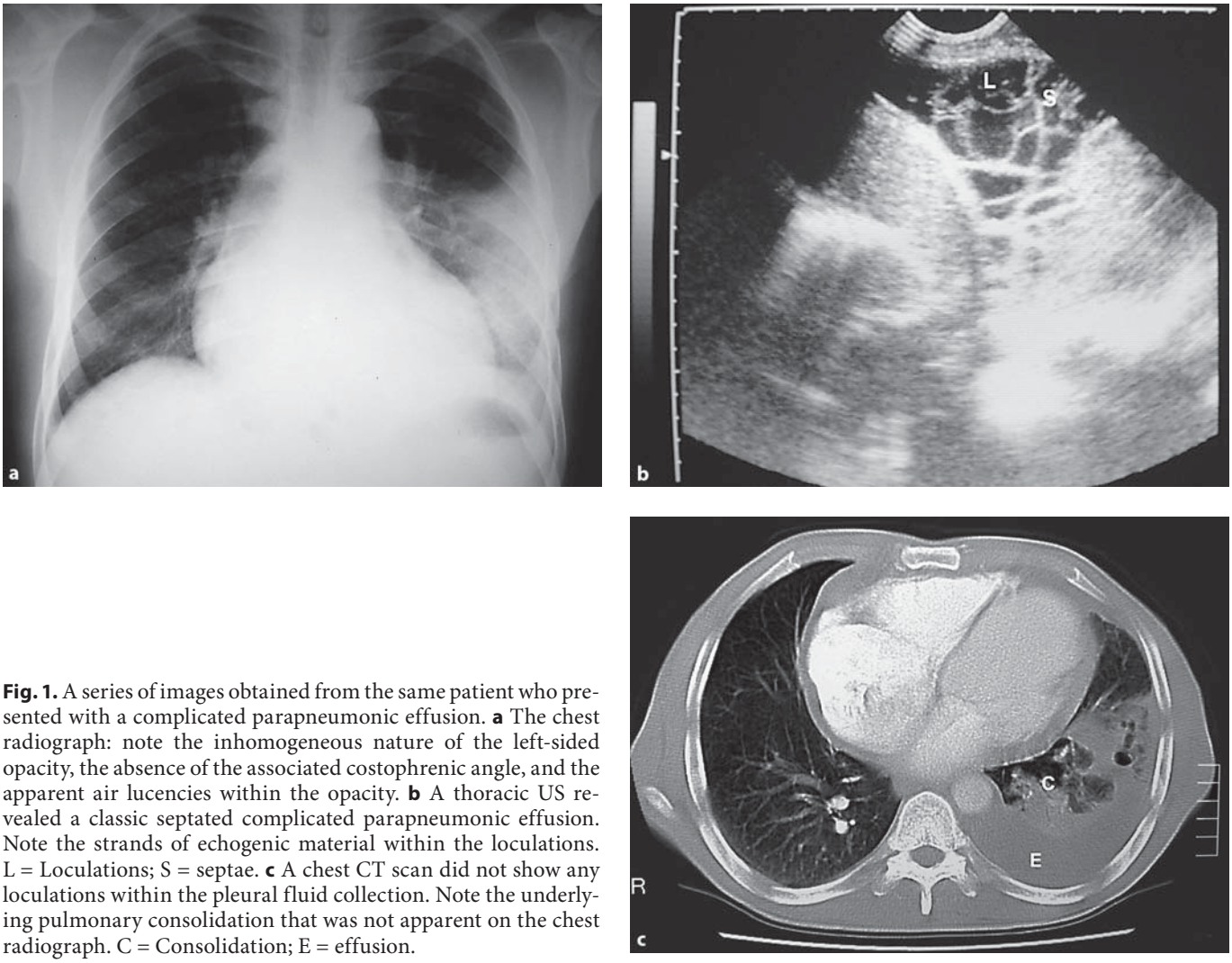

Fig. 1. A series of images obtained from the same patient who presented with a complicated parapneumonic effusion. **a** The chest radiograph: note the inhomogeneous nature of the left-sided opacity, the absence of the associated costophrenic angle, and the apparent air lucencies within the opacity. **b** A thoracic US revealed a classic septated complicated parapneumonic effusion. Note the strands of echogenic material within the loculations. L = Loculations; S = septae. **c** A chest CT scan did not show any loculations within the pleural fluid collection. Note the underlying pulmonary consolidation that was not apparent on the chest radiograph. C = Consolidation; E = effusion.

cluded other streptococci, *Haemophilus influenzae*, enterobacteria, *M. tuberculosis*, and *Nocardia*. The same investigators previously reported that nosocomial pleural infections were most commonly caused by methicillin-resistant *Staphylococcus aureus* (27%), other staphylococci (22%) and enterobacteria (20%) [16].

Clinical Presentation

The presenting symptoms of complicated parapneumonic effusions and empyema can vary significantly and can be dominated by the preceding infective process. Immunocompetent patients with aerobic infections tend to be more acutely ill, and the clinical presentation is similar to pneumonia. This is followed by a 'non-resolving pneumonia' picture with pleuritic chest pain, fever spikes and a failure to improve on apparently adequate antibiotic therapy. Elderly individuals, immunocompromised patients and those with anaerobic infections can have a more indolent course, and may present with weight loss, cough, unexplained fever and anaemia [1].

Diagnosis

Imaging

The chest radiograph usually shows a small to moderate pleural effusion with or without parenchymal infiltrates (fig. 1a). There may be evidence of loculations and air-fluid levels. Longstanding empyema may sometimes cause isolated rounded pleural opacities, which may be

confused with malignant pathology. It was once considered standard practice to request a lateral decubitus radiograph on all patients with suspected pleural sepsis and to use the lateral thickness of the effusions on these films to guide the decision on the need for a thoracentesis [1, 2]. Light et al. [17] showed that pleural effusions less than 1 cm thick on these radiographs resolved with antibiotic therapy alone and did not require pleural aspiration thoracentesis. Thoracic ultrasound (US), however, is an attractive alternative to a lateral decubitus film, as it can very accurately measure the extent of pleural effusions and yields significantly more information regarding the state of the pleural space [18, 19].

The routine use of thoracic US in patients with suspected pleural sepsis should be encouraged. US is particularly helpful in determining the nature of localized or diffuse pleural opacities, and is more sensitive than decubitus expiratory films in identifying small or loculated effusions [18, 19]. Complicated parapneumonic effusions are associated with floating strands of echogenic material which shows mobility with the respiration cycle and denotes advancing stage and chronicity. Complicated effusions may be subdivided into either septated or nonseptated effusions (fig. 1b). The presence of septae is clinically relevant: Chen et al. [20] demonstrated that patients with septated effusions needed longer chest tube drainage, longer hospital care, and were more likely to require fibrinolytic therapy or surgery compared with those with unseptated effusions. Tu et al. [21] confirmed these findings in medical intensive care unit patients. Empyema with high viscosity may cause a strongly echogenic effusion that can be mistaken for a solid pleural lesion. A change in shape during respiratory excursion and the presence of movable strands or echo densities are signs in favour of empyema [22]. Furthermore, thoracic US is invaluable in guiding pleural aspirations and drainage and is superior to chest radiographs at identifying the optimal site for diagnostic thoracentesis [23]. The success rate of US-guided thoracentesis can be as high as 97%. US guidance also decreases the risk of complications following pleural procedures [24].

A thoracic computed tomography (CT) scan may be indicated to better delineate pulmonary and pleural anatomy, particularly if there is a suspicion of an alternative diagnosis (e.g. bronchogenic carcinoma) or prior to surgical intervention [25]. It should be appreciated that loculations within a collection are best appreciated on US, and often not seen on a chest CT scan (fig. 1c). However, collections in interlobar spaces and those adherent to the paramediastinal pleura may escape detection by US and may only be visible on a CT scan (fig. 2: the small paravertebral collection will not be detected on ultrasound). Thickening of the parietal pleura (fig. 2) on a contrasted CT scan is suggestive of empyema [26] and thus an indication for thoracentesis, even in the presence of relatively small pleural collections.

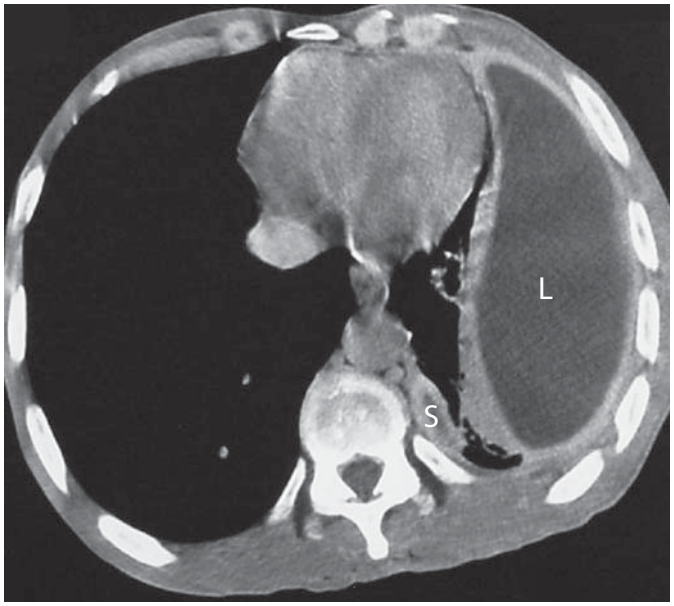

Fig. 2. A CT scan of a patient with empyema showing marked pleural thickening with enhancement, as well as volume loss of the left hemithorax (L, large collection). Also note the second, much smaller, left paravertebral pleural collection (S).

Diagnostic Thoracentesis

All but small (<10 mm on US or lateral decubitus radiograph), free-flowing parapneumonic effusions should be aspirated for diagnostic purposes [27]. Apart from the routine chemistry, cytology and cell count analysis fluid should be sent off for a Gram stain and culture, and pleural fluid pH should be measured by means of a blood gas machine (not a pH meter or an indicator strip) [1]. A positive result from either the Gram stain or culture, or a pH of <7.20 is associated with a worse outcome and indicates the need for drainage [27, 28]. If the pleural fluid pH is unavailable, the pleural fluid glucose may serve as a surrogate. A glucose level >3.4 mmol/l (60 mg/dl) is associated with a better prognosis [1]. Pleural fluid adenosine deaminase is usually elevated in bacterial parapneumonic effusions and empyema, which are neutrophilic in nature. In the setting of a lymphocytic effusion, however, an elevated pleural adenosine deaminase is highly suggestive of a tuberculous effusion, even in low prevalence areas [25, 29, 30].

Table 1. Risk of poor outcome in patients with parapneumonic effusions and empyema

Category	Pleural space anatomy		Pleural fluid chemistry		Pleural fluid bacteriology	Risk of poor outcome	Drainage
1	Minimal, free-flowing effusion (<10 mm)	and	pH unknown	and	Gram stain and culture results unknown	very low	no
2	Small to moderate free-flowing effusion (≥10 mm and <½ hemithorax)	and	pH ≥7.20	and	negative Gram stain and culture	low	no
3	Large, free-flowing effusion (≥½ hemithorax), loculated effusion, or effusion with thickened parietal pleura	or	pH <7.20	or	positive Gram stain and/or culture	moderate	yes
4	Empyema				pus	high	yes

Adapted from the American College of Chest Physicians' consensus statement on the Medical and Surgical Treatment of Parapneumonic Effusions [27]. Note that the presence of frank pus indicates need for drainage irrespective of pH.

Management

Principles

The treatment options for parapneumonic effusions range from non-invasive antibiotic therapy and observation, to semi-invasive techniques such as therapeutic aspiration, tube thoracostomy and intrapleural fibrinolytics, to invasive interventions such as thoracoscopy, thoracotomy or open drainage [1]. In practical terms, however, the initial evaluation should focus on three critical questions, namely: (1) Should the pleural space be drained? (2) How should the pleural space be drained? (3) Should fibrinolytics be instilled? Table 1 is adapted from the American College of Chest Physicians' (ACCP) consensus statement that categorizes parapneumonic effusions according to the need for drainage [25]. It is important to realize that the pleural space anatomy (best visualized by means of US), pleural fluid appearance and smell, as well as pleural pH are often the only useful criteria for initial decision making, as all other laboratory tests need time for processing. Frank pus on aspiration, large effusions greater than half of one hemithorax, effusions with loculations (see fig. 2), or fluid with a pH <7.20 all herald the need for immediate drainage. Further indications include a positive Gram stain, a positive microbial culture and pleural fluid glucose of <3.4 mmol/l (60 mg/dl).

Antibiotics

The initial antibiotic cover of patients with parapneumonic effusions is generally dictated by treatment guidelines for pneumonia, and is altered according to blood and pleural fluid microbial cultures and antibiotic sensitivities. Empirical anaerobic antibiotic cover is generally advised [2], as there may be an anaerobic co-infection which is generally not as amenable to culture as aerobes. Choices in community-acquired empyema include intravenous amoxycillin with clavulanic acid or a combination of a second generation cephalosporin (e.g. cefuroxime) and metronidazole [31]. Clindamycin monotherapy is an effective alternative for patients with a β-lactam allergy. Patients with nosocomial empyema need adequate Gram-negative cover. Possible choices include carbapenems, antipseudomonal penicillins (e.g. piperacillin/tazobactam), or third or fourth generation cephalosporins (e.g. ceftazidime, cefepime) with metronidazole [31]. Vancomycin, linezolid or alternatives may have to be added for suspected or proven methicillin-resistant *S. aureus* infections. Aminoglycosides demonstrate poor pleural penetration and reduced efficacy in acidic environments and should thus be avoided [32].

Observation

ACCP category 1 (table 1) effusions may be observed without a diagnostic aspiration, as the risk of a complicated course is remote [11]. All other cases require at least a diagnostic pleural aspiration before this decision can be made: only category 2 effusions may be observed without formal drainage. There should be no delay in draining category 3 and 4 effusions, as a free-flowing effusion may become loculated in a matter of 1 day.

Therapeutic Thoracentesis

A once-off US-guided therapeutic thoracentesis is an initial treatment option for moderately sized effusions involving less than one hemithorax, in the absence of empyema or a pH <7.20. It may serve as both diagnostic and, if no re-accumulation occurs, definitive management. Recurrent therapeutic pleural aspirations for empyema or complicated parapneumonic effusions have been largely abandoned, although Simmers et al. [23] showed that they were able to successfully treat 24 of 29 patients with parapneumonic effusions by means of alternate day US-guided pleural aspirations. Major disadvantages of this technique seem to be the high number of necessary aspirations and the long hospital stay, as a mean of 7.7 aspirations in 31 days was needed in their study.

Tube Thoracostomy

Indications for chest tube drainage include empyema, complicated parapneumonic effusions (pH <7.20, loculations or positive bacteriological investigations) and large effusions (more than half of a hemithorax involved) [27]. This is most commonly achieved by a standard (24–28 french) intercostal chest drain that is positioned in the dependent part of a free-flowing pleural effusion (most often the posterior costophrenic recess). Insertions are best guided by US, as thickened parietal pleura, adhesions or loculations often complicate insertion. Common sense suggests that smaller bore drains are likely to fail in the presence of pus with a high viscosity. However, some prospective studies have found that 8- to 12-french pigtail catheters or 10- to 14-french catheters inserted with the Seldinger technique under US or CT guidance were at least as effective as larger catheters inserted without imaging [33–35]. However, the positioning of the catheter tips with guidance is likely to be superior compared to blind insertion, irrespective of drain size. Most of these studies also employed a strict rinsing schedule (often several times a day), which might be difficult to sustain in everyday clinical practice. Moreover, a very recent study found a failure rate of 19% with small-bore catheters and concluded that the threshold for using fibrinolytics and large-bore catheters should be low in empyema [36].

Thrombolytics

Complicated parapneumonic effusions and empyemas are characterized by a procoagulant state within the pleural space which results in the progressive development of dense layers of fibrin and loculations. It therefore seems highly plausible that intrapleural fibrinolytics given early in the fibronopurulent phase should prevent loculations and promote pleural drainage. In fact, Tillett and Sherry [37] described the use of streptokinase and streptodornase for this very indication as early as 1949. Unjustified fears of systemic side effects and a paucity of controlled clinical trials have unfortunately delayed the compilation of an evidence base for the use of this modality for many years.

Numerous case series and controlled trials have shown that intrapleural fibrinolysis is safe, increases drainage and improves radiological appearance. A randomized controlled study by Davies et al. [38] established that systemic fibrinolysis or bleeding complications did not occur with streptokinase, and that patients who were given intrapleural streptokinase drained significantly more pleural fluid both during the days of treatment ($n = 24$; mean 391 vs. 124 ml, $p < 0.001$) and overall. Patients who received fibrinolytics also showed greater improvement on the chest radiograph at discharge.

Bouros et al. [39] demonstrated that urokinase was a safe intrapleural fibrinolytic. The same group showed that streptokinase and urokinase were clinically and radiologically equally effective as intrapleural fibrinolytics [40], and that intrapleural urokinase decreased the duration of hospitalization, duration of pleural drainage and time to defervescence. Furthermore, Bouros et al. [41] were able to show that urokinase's effect in empyema was through the lysis of pleural adhesions, rather than the volume effect of instilled urokinase and saline.

Lim and Chin [42] evaluated the efficacy of three different treatment protocols, namely simple chest tube drainage, adjunctive intrapleural streptokinase, and an aggressive empirical approach incorporating streptokinase and early surgical drainage in patients with pleural empyema and high-risk parapneumonic effusions. In this non-randomized, prospective, controlled series they found that the average duration of hospital stay and mortality in both the streptokinase and early surgical drainage group was significantly shorter than with tube drainage alone. The authors concluded that an empirical treatment strategy which combines adjunctive intrapleural fibrinolysis with early surgical intervention resulted in shorter hospital stays and possible reduced mortality in patients with pleural sepsis.

The most meaningful clinical endpoint, that of the necessity for surgical intervention, was only recently addressed in randomized controlled studies. Tuncozgur et al. [43] found a significantly lower decortication rate (60 vs. 29.1%, $p < 0.01$) and shorter duration of hospitalization (14 vs. 21 days, $p < 0.01$) with urokinase than with

placebo. A single-centre, randomized, placebo-controlled study by Diacon et al. [44] used structured clinical protocols for inclusion and evaluation and demonstrated that intrapleural streptokinase resulted in faster resolution of infection, reduced need for surgery (13.6 vs. 45.5%, $p = 0.018$) and improved clinical outcome in patients with loculated parapneumonic effusions and empyema.

The largest prospective double-blind controlled study on the role of intrapleural streptokinase for pleural infection was published in 2005 (MIST 1) [15]. In this study 454 patients with pleural pus, pleural sepsis with a pH <7.2 or bacterial invasion of the pleural space were randomly assigned to receive streptokinase or placebo. The patients included were older than in most other studies (average age 60 years) and had a high prevalence of comorbidities. The MIST 1 study could not substantiate the role of streptokinase in pleural infections: There was no difference in mortality, need for surgery, radiographic outcome or length of hospitalization. The design and execution of this study, however, were criticized [45–47]. The lack of image-based selection criteria meant that patients with pleural sepsis were included irrespective of presence, quantity and quality of loculations. Questions were raised about the reproducibility of clinical management decisions taken across 52 study centres, many of which lacked on-site surgical expertise and contributed only small numbers of patients. The study permitted small-bore chest tubes, but did not report on pleural drainage volumes, which casts doubt on the efficacy of the drainage techniques used. Furthermore, owing to the decentralized and blinded design streptokinase/placebo was shipped to the study centres after randomization causing delays in the initiation of treatment. The value of mortality as an endpoint was also questioned, as patients with serious concomitant illnesses that made survival beyond 3 months unlikely were excluded from the study. The 3-month mortality after hospitalization for pneumonia among middle-aged and older patients is more closely associated with the fact that an episode of pneumonia often identifies a fragile underlying health status than with the severity of the acute episode of pneumonia itself [45]. Intrapleural streptokinase may therefore not have been given a fair chance to improve the short-term mortality [45]. These deficiencies do not invalidate this large randomized trial, but concerns remain about the validity of its results with regards to younger, more severely ill patients and in different health care settings.

The most recent and second largest prospective study was conducted by Misthos et al. [48]. In their study patients were randomized to a group managed solely with tube thoracostomy or a group treated with a combination of tube thoracostomy and streptokinase instillation (no placebo control). They found that tube thoracostomy was successful in 67.1% of cases, whereas the installation of streptokinase led to a favourable outcome in 87.7% ($p < 0.05$) and significantly shortened hospital stay. The mortality rate was also significantly lower in the fibrinolytic group, and streptokinase was found to decrease the rate of surgical interventions and the length of hospital stay.

Tokuda et al. [49] published a meta-analysis of all the major placebo-controlled studies on intrapleural fibrinolysis prior to publication of the study by Misthos et al. Albeit they were able to demonstrate a trend towards improved survival and a decreased need for surgical interventions, the differences failed to become statistically significant.

Clinical trials on the efficacy of recombinant tPA and DNase are currently being performed. An interesting ex vivo observation by Light et al. [50] was that DNase combined with streptokinase (known as Varidase) was superior to either streptokinase or urokinase at liquefying empyemic pleural material obtained from rabbits. It was postulated that the streptodornase (DNase) was necessary for the liquefaction of the deoxyribose nucleoproteins, which make up a sizable proportion of the solid sediment of purulent exudates.

In conclusion, current evidence suggests that intrapleural fibrinolytics cannot be recommended as the standard treatment of parapneumonic effusion and empyema. There seems to be a place for fibrinolytics in the early management of loculated (complicated) parapneumonic effusions and empyema, particularly in young, acutely ill patients, poor surgical candidates and in centres where surgical facilities are limited. Streptokinase and urokinase are presumably equally effective and safe. The efficacy of tPA and DNase still needs to be established. The suggested dosages of the current fibrinolytics in use are summarized in table 2.

Thoracoscopy

Thoracoscopy remains a treatment option for the patient with an incompletely drained loculated parapneumonic effusion, provided that it is performed early in the disease and that the pleural anatomy is defined by means of either US or CT scan [51, 52]. Loculations can be broken down, the visible pleural space completely drained,

Table 2. Intrapleural fibrinolytics – practical use

Fibrinolytic	Dose	Instillation[1]	Duration
Streptokinase	250,000 IU	100–200 ml saline	daily for up to 7 days (until drainage <100 ml/day)
Urokinase[2]	100,000 IU	100 ml saline	daily for up to 3 days
tPA	10–25 mg	100 ml saline	twice daily for up to 3 days

[1] Drain should be clamped for approximately 2 h following installation of fibrinolytics.
[2] Urokinase is no longer universally available.

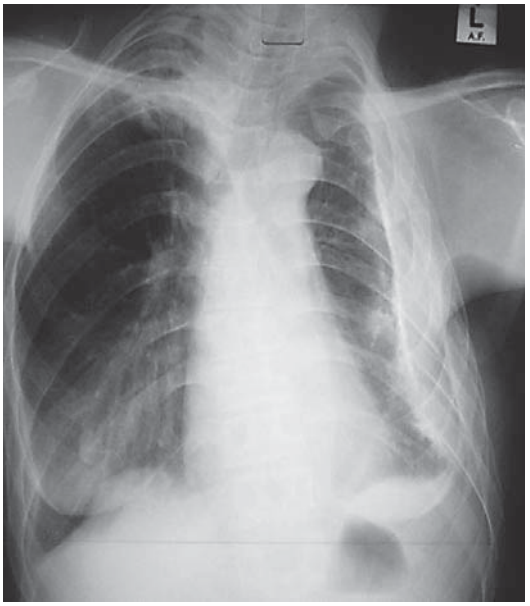

Fig. 3. A chest radiograph showing the long-term sequelae of empyema. Note the formation of a thick pleural peel with volume loss and incarceration of the left lung causing restrictive impairment.

and an intercostal chest tube can be optimally placed [1]. Furthermore, visual inspection of the pleura may guide decisions regarding the need for an open surgical procedure [1].

The exact point where thoracoscopy becomes useful in the management of pleural sepsis remains unclear and is even less well defined than the role of fibrinolytics. Several small retrospective and unblinded prospective studies suggest that thoracoscopy is superior to fibrinolysis [51–54], with the need for thoracotomy or thoracostomy almost halved [53]. At least one study performed on a paediatric population, however, found urokinase to be more cost-effective than routine thoracoscopy [55]. Practically all prospective studies on the role of thoracoscopy [51, 53–55] utilized video-assisted thoracoscopy (VATS), as opposed to medical thoracoscopy. Current evidence does not allow a clear choice between the modalities, and local expertise is likely to dictate the preferred method.

Surgical Management

Open surgery may be required at various stages of the evolution of complicated parapneumonic effusions or empyema. The aim of a procedure in the subacute phase is usually to control sepsis, whereas a procedure in the chronic phase aims to restore chest mechanics by removing a restrictive fibrotic peel encasing the lung (fig. 3).

The main indications for open surgical drainage are failure of medical management to control sepsis in the acute stages of pleural sepsis and failure of tube thoracostomy or thoracoscopy to yield reexpansion of the lung [1, 56]. Thoracotomy with drainage and subsequent closure of the chest with one or more drains left in situ is the standard procedure. Thoracostomy involves incision through the chest wall with rib resection, which produces a stoma with continuous drainage of the chest cavity. In addition, one or more chest tubes can be inserted through the opening, and irrigated daily. The chest tubes can gradually be retracted until complete removal, a process that takes 2–3 months to complete. Drainage from the thoracostomy or from the tubes (cut off close to the skin) can be collected in a colostomy bag. A different approach involves packing the empyema cavity with gauze. A more complex procedure may be performed when the tract between the pleural cavity and the surface of the chest is lined with a skin and muscle flap following rib resection [1]. Drainage is thus achieved without chest tubes with gradual obliteration of the empyema cavity [57].

Decortication is a major surgical intervention that entails the excision of all fibrous tissue from the pleura, with or without the evacuation of associated pus and debris

from the pleural cavity, in order to permit lung reexpansion [58]. It remains a procedure with significant morbidity and a reported mortality of up to 10% [59]. As pleural thickening may resolve over time, decortication is best deferred for up to 6 months [60].

Conclusions: Suggested Management of Parapneumonic Effusions and Empyema

All patients with parapneumonic pleural effusions and empyema require early and adequate antibiotic treatment. Thoracic US should be performed on patients with suspected parapneumonic effusion that is not clearly visualized on a routine postero-anterior chest radiograph. Small, unseptated and free-flowing effusions may be observed, but all other effusions warrant an urgent diagnostic thoracentesis. Sterile effusions with a pH $\geq$7.20 may be observed on antibiotic cover. Empyema and large or loculated effusions need to be drained, as well as parapneumonic effusions with a pH <7.20, glucose <3.4 mmol/l or positive microbial stain and/or culture.

An US-guided therapeutic thoracentesis is an elegant initial treatment option for uncomplicated effusions of moderate size, in the absence of empyema or a pH <7.20, loculations or positive bacteriological investigations. It may serve both as a diagnostic and, if no reaccumulation occurs, definitive procedure. The US evaluation of the pleural cavity will also guide further management. Large bore tube thoracostomy is the treatment option of choice for patients with empyema. Parapneumonic effusions that recur following a single aspiration or cases at high risk should be drained by means of either standard or small-bore intercostal drains.

The use of fibrinolytics remains controversial, although evidence suggests a role for the early use in complicated, loculated parapneumonic effusions and empyema, particularly in young, acutely ill patients, poor surgical candidates and in centres with inadequate surgical facilities. Early thoracoscopy is an alternative to thrombolytics. Local expertise and availability will to a certain extent dictate the initial choice between tube thoracostomy with fibrinolytics or thoracoscopy, although thoracoscopy may also be performed following fibrinolytics if complete drainage is not achieved.

An open surgical drainage procedure will be required for complete drainage where tube thoracostomy or thoracoscopy with associated medical management fails to control pleural sepsis. A surgical decortication may be needed to remove a thick pleural peal and to restore chest mechanics, but this procedure is best deferred for at least 6 months.

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