

Pleural Effusions (parapneumonic effusions, empyema)

Learning Objectives:

1. Know the key parameters in evaluating a pleural effusion to classify exudates vs. transudates.
2. Understand the causes of exudative and transudative pleural effusions.
3. Be familiar with the classification of parapneumonic effusions. Identify the factors which increase the risk for complicated effusions. Define empyema.
4. Know the indications for chest tube drainage, intrapleural thrombolytic therapy and surgical intervention in the management of parapneumonic effusions.
5. Identify the causes of lymphocyte-predominant pleural effusions and be familiar with options for evaluation.

Required Reading:

Bartter T, Santarelli R, Akers S, Pratter MR. The Evaluation of Pleural Effusion. CHEST 1994;106:1209-14.

Light RW. Pleural Effusion. NEJM 2002;346:1971-1977.

Light RW, Rodriguez RM. Management of Parapneumonic Effusions. Clin Chest Med 1998;19(2):373-382.

American College of Chest Physicians. Medical and Surgical Treatment of Parapneumonic Effusions: An Evidence-Based Guideline. (Quick Reference Guide) summarized from CHEST 2000;118: 1158-1171

For Additional Study:

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Heffner JE. Indications for draining a parapneumonic effusion: an evidence-based approach. Sem Resp Infect 1999;14:48-58.

~~Related MKSAP Questions: 7, 25, 32, 43, 53, 55, 58~~



The Evaluation of Pleural Effusion

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ADA=adenosine deaminase; CHF=congestive heart failure; CT=computed tomography; LDH=lactate dehydrogenase; PE=pulmonary embolism; US=ultrasound

Key words: exudates; pleural effusion; thoracentesis; thoracoscopy; transudates

The pleural space normally contains between 7 and 14 ml of fluid.¹ An increased amount of fluid (an effusion) will accumulate in the pleural space whenever the rate of fluid formation exceeds the rate of fluid removal. Increased formation occurs either because of an elevated net hydrostatic pressure gradient (transudation) or because of increased permeability of the pleural vessels (exudation).^{1,2} In addition, fluid can collect in the pleural space via leakage across the diaphragm from the abdomen.¹ Decreased removal occurs if there is a decrease in lymphatic drainage.¹

The purpose of this article is to summarize recent information on the approach to pleural effusion. Emphasis will be on the role of thoracentesis as a diagnostic and therapeutic technique. An overall approach to the patient with undiagnosed pleural effusion is offered.

IMAGING

Normal amounts of pleural fluid are not visible on chest radiographs. Chest radiographs can fail to detect small effusions and do not attain 100 percent sensitivity, even when decubitus views are included, until the amount of pleural fluid exceeds 500 ml.³ In contrast, ultrasonography (US) will detect the presence of as little as 5 to 50 ml of pleural fluid and is 100 percent sensitive for effusions of ≥ 100 ml.³ The superiority of US is particularly apparent for small³ or loculated⁴ effusions; both detection rates and the yield of diagnostic thoracentesis are improved when US is used in this setting, and complication rates may be decreased.⁵

Computed chest tomography (CT) is unequalled in its ability to image the entire pleural space.⁶ (CT also has the advantage of simultaneously imaging the pulmonary parenchyma and mediastinum). Computed tomography is more sensitive than both conventional chest radiography and US for differentiating pleural fluid from pleural thickening and for the identification of focal masses involving the pleura or the chest wall.⁶

In most cases, conventional chest radiography with lateral decubitus views will show the presence and location of pleural effusion.¹ When additional imaging is required to detect pleural effusion, localize it, or guide thoracentesis, US is the preferred technique for reasons of cost, availability, and portability. When more detailed information about the pleural space (and other intrathoracic structures) is required, CT is superior even to US.

INDICATIONS AND CONTRAINDICATIONS TO THORACENTESIS

Thoracentesis can be performed on almost any patient with a pleural effusion. There are no absolute contraindications.¹ Relative contraindications include a bleeding diathesis, systemic anticoagulation, a small volume of pleural fluid, mechanical ventilation, inability of the patient to cooperate, and cutaneous disease such as herpes zoster infection at the needle entry site.⁷

Diagnostic thoracentesis is performed to determine the specific cause of a pleural effusion. Since pathognomonic findings are often absent, efforts have focused on using various characteristics of pleural fluid to guide the subsequent diagnostic approach.^{1,2} Studies of pleural fluid characteristics in patients with diseases of known etiology have been used to develop criteria for separating effusions into transudates and exudates, each of which has a distinct differential diagnosis. These criteria are then used to categorize effusions of unknown etiology as transudates or exudates (Table 1) as the first step in determining a specific etiology.

Not all pleural effusions need to be sampled. For example, if the clinical course is typical, the presence

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Table 1—Pleural Effusions: Differential Diagnoses of Transudates and Exudates^{1,2}

Transudative Effusions	
Congestive heart failure	Atelectasis
Cirrhosis	Myxedema
Nephrotic syndrome	Pulmonary embolism
Peritoneal dialysis	Urinothorax
Exudative Effusions	
Malignancy	Other inflammatory
Lung	Pulmonary embolism
Lymphoma	Dressler's syndrome
Mesothelioma	Asbestos
Metastatic	Uremia
	Trapped lung
Infectious	Radiation therapy
Parapneumonic	Meigs' syndrome
Tuberculous	
Fungal	Lymphatic disease
Viral	Chylothorax
Parasitic	Lymphangiolyomomatosis
Abdominal abscess	Yellow nail syndrome
Hepatitis	
Noninfectious gastrointestinal	Drug-induced
Pancreatitis	Drug-induced lupus
Esophageal rupture	Nitrofurantoin
Abdominal surgery	Dantrolene
Variceal sclerotherapy	Amiodarone
	Methysergide
Collagen vascular disease	Procarbazine
Lupus erythematosus	Practolol
Rheumatoid arthritis	Bromocriptine
Wegener's granulomatosis	Minoxidil
Churg-Strauss syndrome	Bleomycin
Familial Mediterranean fever	Methotrexate
Sjogren's syndrome	Methysergide
Immunoblastic lymphadenopathy	Mitomycin
	Trauma
<i>Diseases That can Present With Transudative or Exudative Effusions</i>	
Pulmonary embolism (usually exudate)	
Diuresed transudate	

of effusion(s) in a patient with congestive heart failure (CHF), small effusion(s) after thoracic or abdominal surgery,⁸ and postpartum effusion⁹ are normally indications for observation, not thoracentesis. However, any time the cause of an effusion or its role in disease is unclear, diagnostic thoracentesis should be performed.

Therapeutic thoracentesis is performed to relieve dyspnea.⁷ Lung volumes increase by a small amount, approximately one third of the volume of fluid withdrawn,¹⁰ and arterial blood gases usually show little change;¹⁰ the relief of dyspnea is believed to be due to a change in the length-tension relationships of the affected diaphragm.¹⁰ Patients with dyspnea unrelieved by therapeutic thoracentesis should not be subjected to additional thoracentesis, chest tube drainage, or attempts at pleurodesis.¹¹

DIAGNOSTIC STUDIES

Table 1 lists the common causes of pleural effusion.

Although the differential diagnosis of pleural effusion is usually separated into transudates vs exudates, some diseases, *eg*, pulmonary embolism, can cause either transudative or exudative effusions.¹²

The classic criteria for transudate vs exudate are those of Light et al.² Fluid is considered exudative if it meets one or more of the following criteria: the absolute pleural fluid lactate dehydrogenase (LDH) level is >200; the pleural:serum LDH ratio is >0.6; and/or the pleural:serum protein ratio is >0.5.²

Several recent articles have evaluated alternate criteria for the separation of transudates from exudates. Two recent studies^{13,14} have suggested that the pleural fluid cholesterol (and pleural:serum cholesterol ratio) level is even more accurate than the criteria of Light et al.² In the studies of Hamm et al¹³ and Valdes et al,¹⁴ a pleural fluid cholesterol level >55 mg/dl was 100 percent specific for an exudative effusion. However, in both studies, the pleural fluid cholesterol level was not 100 percent sensitive; 9.6 percent¹⁴ of patients in one study and 9.7 percent¹³ in the other had exudative effusions with cholesterol levels ≤55 mg/dl.^{13,14} Both studies suggested that the pleural fluid cholesterol separated transudates from exudates more reliably than did the criteria of Light et al applied to the same cases.^{13,14} In the study of Hamm et al,¹³ the criteria of Light et al misclassified 30 percent (9/30) of the transudates (6 met one third and 3 met two thirds of the criteria for an exudate). More recently, Romero et al¹⁵ published a study comparing the criteria of Light et al with cholesterol measurements for 297 pleural effusions. In contrast to the data from Hamm et al and Valdes et al, in their study a pleural fluid cholesterol level >55 mg/dl was not 100 percent specific for an exudate. They found that the criteria of Light et al had a higher accuracy in separating transudates from exudates.

Roth et al¹⁶ looked at the gradient between the serum and pleural albumin levels (serum albumin minus pleural fluid albumin). They found that a gradient <1.2 mg/dl indicated a transudate and a value >1.2 mg/dl indicated an exudate. Fifty-seven of 59 effusions were categorized correctly by the albumin gradient compared with 54 of 59 using the criteria of Light et al.² All five effusions misclassified by the criteria of Light et al were transudates due to CHF that met the criteria of Light et al for exudates. In four of the five, the thoracentesis had followed a period of diuresis. The criteria of Light et al did accurately diagnose two malignant effusions as exudates that had been misclassified as transudates using the albumin criteria.

Meisel et al¹⁷ found that a pleural fluid:serum bilirubin ratio of ≥0.6 had an accuracy equivalent (not superior) to the criteria of Light et al.²

Diuresis can alter pleural chemistries. Recent data show that pleural fluid obtained from patients with CHF after diuresis can be misinterpreted as exudative. Chakko et al¹⁸ performed thoracenteses on patients with effusions due to CHF before and after an average of 6 days of diuresis (SD \pm 2 days). The second thoracentesis showed a significant increase in both protein and LDH levels,¹⁸ and in three of eight cases, postdiuresis chemistries had changed enough to meet the criteria of Light et al² for an exudative effusion.¹⁸ The Roth et al¹⁶ study cited above gives further support to this concept. In contrast, Shinto and Light¹⁹ found that pleural fluid samples obtained from patients with CHF within 48 h of the initiation of diuresis rarely had exudative properties. The combined data suggest that diuresis causes water to leave the pleural space faster than protein and LDH. The longer one waits to obtain pleural fluid after beginning diuresis, the more likely it is that the fluid will have the characteristics of an exudate.

Based on the above studies, it seems clear that the criteria of Light et al² have a high sensitivity and specificity for the separation of transudates from exudates. The criteria of Light et al may lose accuracy for transudates due to CHF after the patient has undergone diuresis; in such a setting, the addition of albumin or cholesterol to pleural fluid studies may improve diagnostic accuracy.

Defining an effusion as a transudate limits the differential diagnosis to a small number of disorders (Table 1). It also ends the need for further diagnostic workup of the pleural effusion itself.

The differential diagnosis of exudative effusions is much broader than that of transudates (Table 1). Sometimes initial fluid studies have one of several characteristics that narrow the differential diagnosis and that will guide further workup (Table 2). Three of the most common causes of exudative effusions are pneumonia, malignancy, and *Mycobacterium tuberculosis*. We shall review some recent data for each of these important causes of exudative pleural effusion.

For parapneumonic effusions, thoracentesis helps confirm the diagnosis and predict the need for chest tube or surgical drainage. Fluid consistent with empyema (gross pus) warrants immediate drainage. The more difficult issue is whether one can predict from the initial thoracentesis which parapneumonic effusions will not resolve with antibiotic therapy and will ultimately require drainage. A "complicated" parapneumonic effusion can be defined as one likely to require chest tube drainage to prevent fibrothorax or to control infection.²⁰ Light et al²¹ initially proposed criteria for such a "complicated" parapneumonic effusion in 1973, but since then, the criteria have been revised²⁰ and revised again.²² There have also been

Table 2—Exudative Pleural Fluid—Differential Diagnoses^{1,2}

	Increased	Decreased
Glucose		<60 Complicated parapneumonic Rheumatoid Malignant Tuberculous Paragonimus
pH		<7.2 Empyema Complicated parapneumonic Rheumatoid Esophageal rupture Tuberculosis Malignancy Paragonimus Hemothorax Systemic acidosis
Amylase	>Upper limit of normal for serum Esophageal rupture Pancreatitis Malignancy	
Red blood cells	Bloody fluid (RBC>100,000/mm ³) Trauma Malignancy Pulmonary embolism Hct>50% of systemic hemothorax	Hct<1% No specificity
Lymphocytes	>50% Lymphoma Other malignancy Chronic infection Tuberculosis Fungi Postpericardiotomy syndrome Sarcoidosis	
Eosinophils	Air in pleural space Blood in pleural space Drug-induced Nitrofurantion Dantrolene Asbestos Malignancy Paragonimus	

data challenging the criteria by showing that some patients with "complicated" parapneumonic effusions may not need chest tube drainage²³ and some patients with "uncomplicated" parapneumonic effusions will eventually require chest tube drainage.²⁴ In addition, Himelman and Callen²⁵ have shown that the presence of loculation is a predictor of increased morbidity independent of fluid characteristics. We concur with the principle that it is better to drain some effusions that may not have required drainage than to leave undrained some effusions that will later

Table 3—Malignancies That Cause Pleural Effusion^{1,2}

Bronchogenic carcinoma
Adenocarcinoma
Lung
Breast
Unknown primary
Prostatic
Gastric
Colonic
Pancreatic
Uterine
Ovarian
Renal
Thyroid
Lymphoma
Cervical
Mesothelioma
Sarcoma

become complicated and possibly increase morbidity, mortality, and length of stay.^{22,25} The data support chest tube drainage for any parapneumonic effusion with evidence of loculation,²⁵ a pH <7.10, a glucose level <40, and/or an LDH level >1,000.^{20,22} An initial pH between 7.1 and 7.29 warrants repeated thoracenteses to see if the pH is dropping or the LDH level is rising.²² If either occurs, chest tube drainage is warranted.²²

It is important to note that there are causes of low pH exudative effusions other than parapneumonic effusions (Table 2), and that low-pH effusions due to these other causes do not warrant chest tube drainage.²⁰ The use of a low pleural fluid pH as an indication for chest tube drainage applies only to parapneumonic effusions.²²

Malignancy is a common and important cause of exudative effusion. Twenty-five percent of all pleural effusions identified in the general hospital setting are due to malignancy.¹¹ Furthermore, the possibility of malignancy is an impetus for further evaluation of an undiagnosed exudate; follow-up shows that 33 percent to 70 percent of exudative effusions undiagnosed after initial thoracentesis and pleural biopsy will eventually prove to be due to malignancy.²⁶⁻²⁸ The finding of a malignant pleural effusion is *de facto* evidence of unresectability of the primary tumor.²⁹ The tumors that most often cause malignant effusions are listed in Table 3.

In 54 percent³⁰ to 63 percent³¹ of patients with malignant effusions, the pleural fluid cytology from the initial thoracentesis will be positive. Obtaining two samples of pleural fluid for cytologic study will increase the yield to about 72 percent, and a third will increase the yield to 77 percent.³¹ While false-positive results almost never occur,³⁰ one must remember that even repeated negative pleural fluid cytologic studies do not rule out malignancy as the cause of the

effusion.^{11,27,28,31-33} Adding pleural biopsy to fluid cytology increases the yield by a modest 7 percent.³⁰

New diagnostic tools may become more clinically important in the near future. For example, Kavuru et al³⁴ used immunocytometry and gene rearrangement analysis on cells from pleural fluid to establish a diagnosis of lymphoma in a patient with negative pleural fluid cytology and unremarkable results of pleural biopsy.³⁴

There have been several recent studies showing that once a malignant pleural effusion has been diagnosed, the pleural fluid characteristics are important as both prognostic indicators and as guides to management.³⁵ A low (<7.30) pH and a low (<60 mg/dl) glucose level are both associated with more extensive pleural involvement with tumor,³⁶ a higher yield on fluid cytology,^{35,37} decreased success rates of pleural sclerosis,³⁵ and shorter survival times.³⁵ In one study, mean survival was 2.1 months for low pH malignant effusions and 9.8 months for normal pH malignant effusions.³⁵

Tuberculous effusion is less common than the above,^{2,27,33} but is important because the diagnosis mandates antituberculous therapy. Acid-fast smears of tuberculous pleural effusions are positive in only 0 percent³³ to 9 percent³⁸ of cases, while fluid cultures are positive in 13 percent³³ to 65 percent³⁹ of tuberculous effusions. Pleural biopsy for pathology (granulomas) and culture increases the yield to about 86 percent.³³ Ocana et al⁴⁰ have suggested that measurement of pleural fluid adenosine deaminase (ADA) levels is of diagnostic value for tuberculous effusions. In their study, an ADA level >50 U/L was 94 percent sensitive and 90 percent specific for tuberculous effusion while an ADA level of <45 U/L was 100 percent sensitive and specific for a nontuberculous etiology.⁴⁰

UNDIAGNOSED EXUDATE

Studies on pleural fluid yield a definitive or presumptive diagnosis in about 74 percent of cases.⁴¹ Even when results of fluid analysis are nondiagnostic, clinically useful information is obtained in most patients.⁴¹ However, the exudative effusion whose cause is still undiagnosed after initial thoracentesis is a common clinical problem. Concern is primarily over the possibilities of either malignancy or tuberculosis.

The patient with an undiagnosed exudative effusion should undergo a repeated thoracentesis and simultaneous pleural biopsy. Cytology studies on the repeated fluid sample will increase the yield for malignancy.³¹ The biopsy is particularly important for tuberculosis but will also slightly increase the yield for malignancy.^{26,30,33} A pleural biopsy specimen

that is culture positive for *M tuberculosis* or that shows granulomas is an indication for antituberculous therapy.

Leslie and Kinasewitz²⁶ have suggested that if a patient with undiagnosed exudates and "nonspecific pleuritis" on biopsy specimen meets six criteria, it is reasonable to follow the patient without further workup of the pleural space, as malignancy and tuberculosis are very unlikely. The patient must (1) be clinically stable, (2) have no weight loss, (3) have a negative PPD, (4) be afebrile (temperature <38°C), (5) have fewer than 95 percent lymphocytes in the pleural fluid, and (6) have an effusion that occupies less than 50 percent of the hemithorax. During a 33-month follow-up of the 87 patients meeting all six of these criteria, one (1.1 percent) was eventually diagnosed as having an effusion due to malignancy (lymphoma), while none developed evidence of tuberculosis.²⁶

For patients with exudative effusion still undiagnosed after the above and with parenchymal abnormalities on chest radiograph or with hemoptysis, bronchoscopy is a useful next step.⁴² In contrast, in the absence of parenchymal abnormalities or hemoptysis, bronchoscopy is not warranted.⁴² The clinical presentation should also be reviewed with pulmonary embolism (PE) in mind if PE has not yet been considered, as PE is a common cause of pleural effusion.¹² If results of bronchoscopy are nondiagnostic or not indicated and if PE is unlikely or ruled out, thoracoscopy should be considered next.

Thoracoscopy was performed frequently in the first half of the 20th century, but then it fell out of favor due to advances in open thoracic surgical techniques.⁴³ Advances in instrumentation have now led to a resurgence in the use of thoracoscopy,⁴⁴ and its role in the diagnosis of exudative pleural effusions continues to evolve. Thoracoscopy will reveal the cause in 92 percent of cases of exudative effusions undiagnosed following the above workup.⁴³ We would recommend thoracoscopy with local anesthesia, conscious sedation, and without intubation.²⁷ Under such conditions, thoracoscopy has the same complication rate as pleural biopsy.²⁷ (We would separate thoracoscopy for pleural disease from "thoracoscopic surgery," the term for more complex thoracoscopic operative procedures.⁴⁵) If thoracoscopy without intubation is not available, we would recommend a second pleural biopsy (and third fluid sampling) before proceeding to thoracoscopy under general anesthesia or to open thoracotomy.^{26,33} In selected patients in whom clinical suspicion for tuberculosis or malignancy was high³³ or who met one or more of the criteria of Leslie and Kinasewitz,²⁶ the yield of second pleural biopsies was 33 percent to 50 percent. Thus, a significant number of patients

may be spared general anesthesia.³³ It is important to note that diagnostic yield will be affected by the incidence of different diseases in different populations.

In the past, open thoracotomy was the most definitive procedure performed in an attempt to determine the cause of an undiagnosed exudative pleural effusion.³² It is assuming a much lesser role since the renaissance of thoracoscopy; thoracoscopy has a similar (or superior) yield and lower morbidity and mortality.^{27,28} Thoracotomy should probably be limited to the occasional patient with an undiagnosed condition with a suspect effusion who cannot undergo thoracoscopy or to patients in whom an open procedure is indicated whatever the results of pleural studies.

After the above, one should have determined a cause for >90 percent of exudative pleural effusions.^{27,28} Sixty percent of patients with exudative effusions undiagnosed after open thoracotomy will experience no progressive illness.³² Most of the remainder will be found to have an underlying malignancy as the cause of their effusion.³² Presumably, the results will be similar for thoracoscopy.

COMPLICATIONS

Thoracentesis historically was perceived as "technically uncomplicated, well tolerated, and quite safe."⁴⁶ Subsequent prospective data have contradicted this impression.^{5,41,47,48} Major complication rates of thoracenteses done by house officers have ranged from 11.6 percent⁴¹ to 30.3 percent.⁵ The most common complication is pneumothorax,^{5,41,47,48} with 3.9 percent⁴¹ to 6.1 percent⁵ of patients requiring chest tube insertion. In addition, in 2 percent to 14.7 percent of diagnostic thoracenteses, little or no fluid is obtained ("inadequate yield").⁴⁸ A decreased rate of serious complications is associated with: operator training and experience,⁴⁸ use of a smaller needle,^{48,49} US guidance,^{5,47} and diagnostic (as opposed to therapeutic) thoracentesis.⁴¹

Re-expansion pulmonary edema can occur with removal of large amounts of pleural fluid, and some favor stopping a therapeutic thoracentesis after removal of 1,000 ml⁵⁰ unless pleural pressures are monitored during removal and remain greater than -20 cm H₂O, in which case removal can continue.⁵⁰ The data are inconclusive, and others drain as much fluid as possible.

Thoracoscopy with conscious sedation has a major complication rate of about 1.9 percent.²⁷ It should be noted that a chest tube is a routine part of the procedure and is not considered a complication.

CONCLUSION

A systematic approach to pleural effusions will generally result in a specific diagnosis and help to guide therapy. Thoracentesis remains an essential

initial step and pleural biopsy (blind or via thoracoscopy) plays an important role in diagnosing exudates.

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Clinical Practice

This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the author's clinical recommendations.

PLEURAL EFFUSION

RICHARD W. LIGHT, M.D.

A 70-year-old man with an 80-pack-year history of smoking and a history of congestive heart failure presents with increasing shortness of breath. He also has aching chest pain on the right side that worsens with deep inspiration. He is afebrile. The chest radiograph reveals bilateral pleural effusions, with more pleural fluid on the right than on the left. How should this patient be evaluated?

THE CLINICAL PROBLEM

Although many different diseases may cause a pleural effusion (Table 1), the most common causes in the United States are congestive heart failure, pneumonia, and cancer. The diagnostic workup of a patient with a pleural effusion will depend on the probable causes of the condition in that patient.

STRATEGIES AND EVIDENCE

Initial Evaluation

The history and the physical examination are critical in guiding the evaluation of pleural effusion. Several aspects of the physical examination should receive special attention. Chest examination typically reveals dullness to percussion, the absence of fremitus, and diminished breath sounds or their absence. Distended neck veins, an S₃ gallop, or peripheral edema suggests congestive heart failure, and a right ventricular heave or thrombophlebitis suggests pulmonary embolus. The presence of lymphadenopathy or hepatosplenomegaly suggests neoplastic disease, and ascites may suggest a hepatic cause.

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TABLE 1. LEADING CAUSES OF PLEURAL EFFUSION IN THE UNITED STATES, ACCORDING TO ANALYSIS OF PATIENTS SUBJECTED TO THORACENTESIS.*

CAUSE	ANNUAL INCIDENCE	TRANSUDATE	EXUDATE
Congestive heart failure	500,000	Yes	No
Pneumonia	300,000	No	Yes
Cancer	200,000	No	Yes
Pulmonary embolus	150,000	Sometimes	Sometimes
Viral disease	100,000	No	Yes
Coronary-artery bypass surgery	60,000	No	Yes
Cirrhosis with ascites	50,000	Yes	No

*Adapted from Light.¹

Since conditions other than pleural effusions may produce similar radiologic findings, alternative imaging studies are frequently necessary to verify that a pleural effusion is present. Ultrasonographic studies or lateral decubitus radiographs are used most commonly, but computed tomographic (CT) scans of the chest allow imaging of the underlying lung parenchyma or mediastinum.

Indications for Thoracentesis

The indication for diagnostic thoracentesis is the presence of a clinically significant pleural effusion (more than 10 mm thick on ultrasonography or lateral decubitus radiography) with no known cause (Fig. 1). If a patient presents with congestive heart failure and bilateral effusions of similar size, is afebrile, and has no chest pain, a trial of diuresis can be undertaken. Since more than 80 percent of patients with pleural effusions caused by congestive heart failure have bilateral pleural effusions,² thoracentesis is indicated if the effusion is unilateral. Approximately 75 percent of effusions due to congestive heart failure resolve within 48 hours after diuresis is begun.² If the effusions persist for more than three days, thoracentesis is indicated.

The initial thoracentesis is usually performed for purposes of diagnosis, unless the patient has shortness of breath when at rest, in which case therapeutic thoracentesis to remove up to 1500 ml of fluid is indicated. Thoracentesis can be performed at the bedside with the aid of diagnostic imaging. Ultrasonographic guidance is indicated if difficulty is encountered in obtaining pleural fluid or if the effusion is small.³ It remains uncertain whether the use of ultrasonography

decreases the incidence of pneumothorax after thoracentesis; the extent of the operator's experience is probably more important than whether ultrasonography is used.¹ It is not necessary to perform chest radiography routinely after thoracentesis unless air is obtained during the thoracentesis; coughing, chest pain, or dyspnea develops; or tactile fremitus is lost over the superior part of the aspirated hemithorax.² In one series of 506 thoracenteses, pneumothorax was present in 13 of the 18 patients with one or more of these symptoms (72 percent) but in only 5 of 488 patients with none of these symptoms (1 percent).⁴

Appearance of the Pleural Fluid

The gross appearance of the pleural fluid provides useful information (Table 2). A bloody appearance of the pleural fluid narrows the differential diagnosis. In a series of 21 cases of pleural effusion with bloody fluid, 12 were due to cancer, 5 to pulmonary embolism, 2 to trauma, and 2 to pneumonia.⁵ Turbidity of the pleural fluid can be caused either by cells and debris or by a high lipid level (Table 2).¹ The odor of the pleural fluid also provides useful information. A putrid odor indicates that the patient probably has an infection due to anaerobic bacteria, and an odor of urine indicates probable urinothorax.¹

Differentiation of Exudates from Transudates

A transudative pleural effusion occurs when pleural fluid accumulates because of an imbalance between the hydrostatic and oncotic pressures. The leading causes of transudative pleural effusions are congestive heart failure, cirrhosis, and pulmonary embolism. In contrast, an exudative pleural effusion occurs when the local factors influencing the accumulation of pleural fluid are altered. The leading causes of exudative effusions are pneumonia, cancer, and pulmonary embolism.

The first step in the evaluation is to determine whether an effusion is transudative or exudative.⁶ If it is exudative, more diagnostic tests are required in order to determine the cause of the local disease, whereas if it is transudative, the physician must establish or rule out a diagnosis of congestive heart failure, cirrhosis, or pulmonary embolism.

For the past several decades, transudates have been differentiated from exudates according to Light's criteria,⁷ by measurement of the levels of protein and

lactate dehydrogenase in the pleural fluid and in the serum (Table 3). Since these criteria were originally published, several alternative measurements have been proposed for making this distinction^{8,9} (Table 3). Light's criteria are the most sensitive for identifying exudates but have lower specificity than other criteria — that is, on the basis of Light's criteria, some patients who actually have transudative pleural effusions will be thought to have exudative pleural effusions. If the clinical appearance suggests a transudative effusion but the pleural fluid is an exudate according to Light's criteria, the difference between the albumin levels in the serum and the pleural fluid should be measured. Almost all patients with a serum albumin level that is more than 1.2 g per deciliter higher than the pleural-fluid albumin level have a transudative effusion.⁹ However, this albumin gradient alone should not be used to distinguish transudates from exudates because it will misidentify approximately 13 percent of exudates as transudates.⁹

For an effusion that is likely to be transudative, initial measurement should be limited to the pleural-fluid protein and lactate dehydrogenase levels.¹⁰ In patients with such effusions, additional tests provide no additional information and sometimes produce misleading results.¹⁰

Evaluation of an Exudative Effusion

Additional tests are needed, however, on exudative pleural fluids. Depending on the clinical presentation, these may include total and differential cell counts, smears and cultures for organisms, measurement of glucose and lactate dehydrogenase levels, cytologic analysis, and testing for a pleural-fluid marker of tuberculosis.

Total and Differential Cell Counts

A predominance of neutrophils in the pleural fluid (more than 50 percent of the cells) indicates that an acute process is affecting the pleura. In one series, 21 of 26 parapneumonic effusions (81 percent), 4 of 5 effusions secondary to pulmonary embolus (80 percent), and 4 of 5 effusions secondary to pancreatitis (80 percent) contained more than 50 percent neutrophils, but only 7 of 43 malignant effusions (16 percent) and none of 14 tuberculous effusions contained more than 50 percent neutrophils.⁵

A predominance of mononuclear cells indicates a

Figure 1 (facing page). Algorithm for the Evaluation of Patients with Pleural Effusion.

Pulmonary embolism should be considered earlier in the evaluation if there are clinical symptoms or signs that suggest this diagnosis (for example, pleuritic chest pain, hemoptysis, or dyspnea out of proportion to the size of the effusion). LDH denotes lactate dehydrogenase.

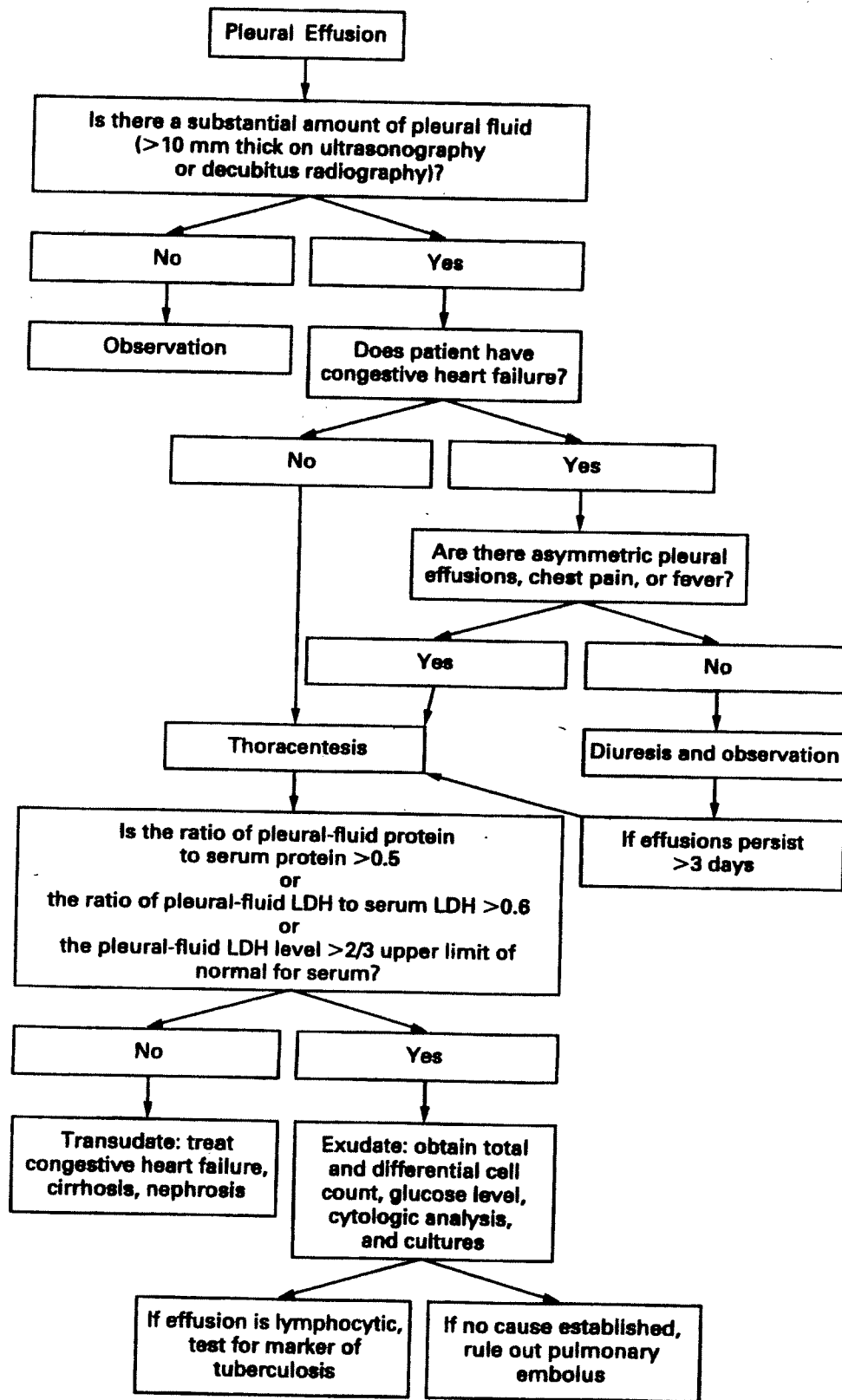


TABLE 2. TESTS INDICATED, ACCORDING TO THE APPEARANCE OF THE PLEURAL FLUID.

APPEARANCE OF FLUID	TEST INDICATED	INTERPRETATION OF RESULT
Bloody	Hematocrit	<1% → nonsignificant 1-20% → cancer, pulmonary embolus, or trauma >50% of peripheral hematocrit → hemothorax
Cloudy or turbid†	Centrifugation	Turbid supernatant → high lipid levels
Turbid supernatant	Triglyceride level	>110 mg/dl → chylothorax >50 mg/dl, but <110 mg/dl → obtain lipoprotein analysis Presence of chylomicrons → chylothorax <50 mg/dl and cholesterol >250 mg/dl → pseudo-chylothorax
Putrid odor	Stain and culture	Putrid odor → possible anaerobic infection

*To convert values for triglycerides to millimoles per liter, multiply by 0.01129. To convert values for cholesterol to millimoles per liter, multiply by 0.02586.

†This appearance is consistent with the presence of either cells and debris or high lipid levels.

TABLE 3. SENSITIVITY OF TESTS TO DISTINGUISH EXUDATIVE FROM TRANSUDATIVE EFFUSIONS.*

TEST	SENSITIVITY FOR EXUDATE	SPECIFICITY FOR EXUDATE
	%	
Light's criteria (one or more of the following three)	98	83
Ratio of pleural-fluid protein level to serum protein level >0.5	86	84
Ratio of pleural-fluid LDH level to serum LDH level >0.6	90	82
Pleural-fluid LDH level >two thirds the upper limit of normal for serum LDH level	82	89
Pleural-fluid cholesterol level >60 mg/dl (1.55 mmol/liter)	54	92
Pleural-fluid cholesterol level >43 mg/dl (1.10 mmol/liter)	75	80
Ratio of pleural-fluid cholesterol level to serum cholesterol level >0.3	89	81
Serum albumin level - pleural-fluid albumin level <1.2 g/dl	87	92

*LDH denotes lactate dehydrogenase.

chronic process. A preponderance of small lymphocytes indicates that the patient most likely has cancer or tuberculous pleuritis, although such a preponderance is also seen in pleural effusions after coronary-artery bypass surgery.^{5,11,12} The combined data from two series^{5,11} show that 90 of 96 exudative pleural effusions consisting of more than 50 percent lymphocytes (94 percent) were due to cancer or tuberculosis. In these series, 90 of 116 tuberculous pleural effusions (78 percent) contained more than 50 percent lymphocytes.^{5,11}

Pleural-fluid eosinophilia (more than 10 percent eosinophils) is caused in about two thirds of cases by blood or air in the pleural space.¹³ Pleural-fluid eosin-

ophilia is uncommon in patients with cancer or tuberculosis, unless the patient has undergone repeated thoracenteses.¹³⁻¹⁵ Unusual causes of eosinophilic pleural effusions include reactions to drugs (dantrolene, bromocriptine, or nitrofurantoin), exposure to asbestos, paragonimiasis, and the Churg-Strauss syndrome.¹

Smears and Cultures

Gram's staining and culture for both aerobic and anaerobic bacteria will identify infected pleural fluids. The yield with culture is increased if blood-culture bottles are inoculated at the bedside with the pleural fluid.¹⁶ If there is a reasonable likelihood that the pa-

tient has mycobacterial or fungal infection — for example, as indicated by a pleural fluid with more than 50 percent lymphocytes or a chronic febrile illness — cultures for these organisms are indicated. Smears of the pleural fluid may reveal fungi, but smears for mycobacteria are rarely positive unless the patient has a tuberculous empyema or the acquired immunodeficiency syndrome.^{14,17}

Pleural-Fluid Glucose Level

The presence of a low pleural-fluid glucose concentration (less than 60 mg per deciliter) indicates that the patient probably has a complicated parapneumonic¹⁸ or a malignant effusion.^{19,20} Less common causes of low-glucose pleural effusions are hemothorax, tuberculosis, rheumatoid pleuritis, and more rarely, the Churg–Strauss syndrome, paragonimiasis, and lupus pleuritis.¹

Pleural-Fluid Lactate Dehydrogenase Level

The level of lactate dehydrogenase in the pleural fluid correlates with the degree of pleural inflammation and should be measured each time pleural fluid is sampled from a pleural effusion whose cause has not been determined. A lactate dehydrogenase level that increases with repeated thoracentesis suggests that the degree of inflammation is increasing, and a diagnosis should be aggressively pursued.¹ Conversely, if the lactate dehydrogenase level in the pleural fluid decreases with repeated thoracentesis, a less aggressive diagnostic approach may be considered.

Pleural-Fluid Tests for Cancer

Cytologic examination of the pleural fluid is a fast, efficient, and minimally invasive means for establishing a diagnosis of cancer. Yields on cytologic examination are increased if both cell blocks and smears are examined. If a patient has metastatic adenocarcinoma, cytologic analysis will establish the diagnosis in more than 70 percent of cases.^{5,21} Cytologic analysis is less efficient at establishing the diagnosis of cancer if the patient has a mesothelioma (sensitivity, 10 percent), squamous-cell carcinoma (20 percent), lymphoma (25 to 50 percent), or a sarcoma (25 percent) involving the pleura.¹ Since a blind needle biopsy of the pleura adds little to cytologic analysis in terms of diagnosing pleural cancer,²¹ thoracoscopy is the procedure of choice for patients with suspected cancer and negative results on cytologic examination. Cytologic testing is not routinely warranted in young patients with evidence of acute illness.

If lymphoma is suspected, flow cytometry can establish the diagnosis by demonstrating the presence of a clonal cell population in the pleural fluid.²² Measurement of the levels of tumor markers in the pleural

fluid has proved disappointing in establishing the diagnosis of pleural cancer.²³ If the cutoff level is set sufficiently high so that there are no false positives, the sensitivity of the test is less than 50 percent.

Pleural-Fluid Markers of Tuberculosis

If tuberculous pleuritis is not treated, the effusion will resolve, but pulmonary or extrapulmonary tuberculosis subsequently develops in more than 50 percent of patients.²⁴ Evaluation for tuberculosis is warranted if there is pleural-fluid lymphocytosis. Since less than 40 percent of patients with tuberculous pleuritis have positive pleural-fluid cultures,¹² alternative means, such as the measurement of adenosine deaminase or interferon- γ or the polymerase chain reaction (PCR) for mycobacterial DNA, are used to establish the diagnosis. In one study, the pleural-fluid adenosine deaminase level was above 40 U per liter in 253 of 254 patients with tuberculous pleuritis (99.6 percent) and below this cutoff point in 102 of 105 patients with lymphocytic pleural effusions from other causes (97.1 percent).²⁵ A pleural-fluid interferon- γ level of 140 pg per milliliter is comparable to an adenosine deaminase level of 40 U per liter in terms of diagnosing tuberculous pleuritis.²⁶ If DNA from *Mycobacterium tuberculosis* is detected in the pleural fluid by PCR, the diagnosis of tuberculous pleuritis is established.²⁷

Other Tests on the Pleural Fluid

Other diagnostic tests on the pleural fluid are indicated in specific situations. Measurement of the pleural-fluid pH (with the use of a blood-gas machine) is warranted if a parapneumonic or malignant pleural effusion is suspected. A pleural-fluid pH below 7.20 in a patient with a parapneumonic effusion indicates the need for drainage of the fluid.²⁸ A pleural-fluid pH in this range in a patient with a malignant pleural effusion suggests that the patient's life expectancy is only about 30 days and that chemical pleurodesis is likely to be ineffective.¹

An elevated pleural-fluid amylase level is seen in patients with pancreatic disease and esophageal rupture.²⁹ Amylase should therefore be measured if there are clinical symptoms or if the history suggests one of these diagnoses. In the absence of these indications, routine pleural-fluid amylase determinations are not useful.²⁹

Immunologic tests on the pleural fluid, such as the determination of antinuclear antibody titers³⁰ or rheumatoid factor levels, add little diagnostic information; the diagnosis of lupus pleuritis or rheumatoid pleuritis is established by the clinical picture and the antinuclear antibody and rheumatoid factor levels in the serum. In addition, antinuclear antibody measurements were falsely positive at a high titer in 13 of

145 patients with effusions that were not caused by lupus (9 percent).³⁰

Evaluation for Pulmonary Embolism

The possibility of pulmonary embolus should be considered if a patient has pleuritic chest pain, hemoptysis, or dyspnea out of proportion to the size of the effusion. The best screening test is measurement of the level of D-dimer in the peripheral blood.³¹ There are many different D-dimer tests available with varying sensitivities and cutoff levels³¹; if a sensitive D-dimer test is used and it is negative, the diagnosis of pulmonary embolism is essentially ruled out. If the D-dimer test is positive, then additional specific diagnostic testing — such as duplex ultrasonography of the legs, spiral CT, perfusion scanning of the lungs, or pulmonary arteriography — is necessary to establish the diagnosis.

Pleural Effusion of Unknown Cause

The cause of the effusion remains unclear in the cases of a substantial percentage of patients with exudative effusions after the history, physical examination, and analysis of pleural fluid.³² If the effusion persists despite conservative treatment, thoracoscopy should be considered, since it has a high yield for cancer or tuberculosis. If thoracoscopy is unavailable, alternative invasive approaches are needle biopsy and open biopsy of the pleura. No diagnosis is ever established for approximately 15 percent of patients despite invasive procedures such as thoracoscopy or open pleural biopsy.

AREAS OF UNCERTAINTY

It is uncertain whether the use of ultrasonography as an aid in performing thoracentesis decreases the likelihood of pneumothorax.^{33,34} The best approach to diagnosing pulmonary embolus in patients with pleural effusion is not clear. There is controversy about whether patients with a lymphocytic pleural effusion should be treated for pleural tuberculosis solely on the basis of an elevated level of adenosine deaminase in the pleural fluid. Although I would recommend performing a battery of tests in patients with exudative pleural effusions of which the cause remains undiagnosed, no prospective study has been performed to evaluate the cost effectiveness of such an approach.

GUIDELINES

There are no formal guidelines dealing directly with the evaluation of pleural effusion of unknown cause.

CONCLUSIONS AND RECOMMENDATIONS

A thoracentesis should be performed in patients with a pleural effusion of unknown cause unless the effusion is small (less than 10 mm on ultrasonography) or the patient has congestive heart failure and bi-

lateral pleural effusions. Ultrasonographic guidance for the thoracentesis is indicated if the effusion is small or if difficulty is encountered in obtaining fluid. If it is likely that the patient has a transudative pleural effusion, the only laboratory tests indicated are measurements of the lactate dehydrogenase and protein levels in the pleural fluid. If a patient has an exudative effusion, as indicated by a ratio of the pleural-fluid protein level to the serum protein level of more than 0.5, a ratio of the pleural-fluid lactate dehydrogenase level to the serum lactate dehydrogenase level of more than 0.6, or a pleural-fluid lactate dehydrogenase level that is more than two thirds the upper limit of normal for the serum lactate dehydrogenase level, the pleural fluid should be stained with Gram's stain and cultured for bacteria. In addition, the following tests should usually be performed on exudative pleural fluid: total and differential cell counts, measurement of the glucose level, an assay for a pleural-fluid marker of tuberculosis (if the effusion is predominantly lymphocytic), and cytologic analysis.

If no diagnosis is evident after this initial evaluation, the possibility of pulmonary embolus should be evaluated; this diagnosis should be pursued earlier if the clinical presentation is suggestive of this condition. If the diagnosis remains unclear, consideration should be given to performing more invasive tests, such as thoracoscopy, needle biopsy of the pleura, or open pleural biopsy.

In the case described in the vignette, congestive heart failure is a possibility, since the patient had a history of this condition. However, given the fact that the effusions are of unequal size and that chest pain is present, thoracentesis is indicated. An exudative effusion is an indication for cytologic testing, since cancer is a particular concern given the patient's age and history of heavy smoking. If the cytologic examination is nondiagnostic, thoracoscopy or another invasive evaluation should be considered.

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MANAGEMENT OF PARAPNEUMONIC EFFUSIONS

Richard W. Light, MD, and R. Michael Rodriguez, MD

The annual incidence of bacterial pneumonia in the United States is estimated at 4 million and approximately 20% of those cases require hospitalization.³² The incidence of parapneumonic effusion in patients hospitalized with pneumonia is about 40%.²⁵ The morbidity and mortality rates in patients with pneumonia and pleural effusions are greater than in patients with pneumonia alone. In one recent study,¹⁶ the relative risk of mortality in patients with community-acquired pneumonia was 7.0 times higher for patients with bilateral pleural effusions and 3.4 times higher for patients with unilateral-pleural effusion of moderate or greater size compared with other patients with community-acquired pneumonia. Delay in instituting proper therapy for effusions is responsible for much of the increased morbidity and mortality.

DEFINITIONS

Any pleural effusion associated with bacterial pneumonia, lung abscess, or bronchiectasis is a parapneumonic effusion.²⁶ An empyema, by definition, is pus in the pleural space. Pus is thick, purulent-appearing pleural fluid. A complicated-parapneumonic effusion is a parapneumonic effusion for which tube thoracostomy is necessary for resolution. A loculated parapneumonic effusion is a parapneumonic effusion that is not free-flowing. A

multiloculated parapneumonic effusion is a loculated-parapneumonic effusion with more than one compartment.

HISTORY

Writings on the treatment of empyema date back to around 500 BC, when Hippocrates recommended treating empyema with open drainage.¹ At that early time, Hippocrates recognized that the prognosis of the patient depended on the characteristics of the fluid. He wrote the following: "Those cases of empyema are treated by incision or the cautery, if the water flows rapidly all at once certainly prove fatal. When empyema is treated, either by the incision or the cautery, if pure and white pus flows slowly from the wound, the patients recover."

The treatment of empyema remained essentially unchanged from the time of Hippocrates until the middle of the nineteenth century. At that time, Trousseau⁵¹ in France and Bowditch⁸ in the United States popularized the use of thoracentesis and demonstrated that open drainage was not necessary in many cases. The next advance was provided by Hewitt,¹⁷ who described a method of closed drainage of the chest in which a rubber tube was placed into the empyema cavity through a cannula. He was the first to use the water-seal for chest tubes.

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When dealing with an empyema, the management of the empyema cavity poses a significant problem. In the 1890s, articles by Estlander¹¹ and Schede³⁸ described thoracoplasty as a means of obliterating the empyema cavity. Thoracoplasty involves the resection of the ribs, intercostal muscles, and parietal pleural peel over the cavity. The remaining defect is covered by the few remaining muscles, the scapula, and the subcutaneous tissue and skin. At approximately the same time, Fowler¹³ and Beck⁵ initially described decortication. With decortication, all pus is removed from the pleural space and all the fibrous tissue is removed from the visceral and parietal pleura.

Hippocrates had recognized before the birth of Christ that open drainage procedures were dangerous if the empyema fluid was not thick.¹ Paget³⁴ again emphasized in 1896 that open drainage should not be instituted for empyema before at least the fifteenth day of the illness. Yet, by World War I, open drainage had become the accepted treatment for all cases of parapneumonic effusions. During World War I, there was a high incidence of parapneumonic effusions in American soldiers and the treatment of all such patients with open drainage had disastrous results. The United States Surgeon General, in 1919, found that the average mortality of individuals with pleural infections was 30.2% and, in some hospitals, the mortality rate was as high as 70%.¹⁵ The explanation for the high mortality rate was that the open drainage procedure was performed too early, resulting in collapse of the underlying lung. *Streptococcus hemolyticus* was responsible for many of those cases and that organism characteristically produces a large nonloculated pleural effusion.³³

An empyema commission headed by Evarts Graham was formed to address the high mortality rates. Graham¹⁴ demonstrated that when dogs with experimental empyema were treated by the early insertion of open chest tubes, the mortality rate was higher and deaths occurred earlier than in dogs that were not treated with chest tubes. The empyema commission made the following recommendations: (a) The pleural fluid should be drained, but one must avoid an open pneumothorax in the acute-pneumonic phase; (b) care should be taken to avoid a chronic empyema by rapid sterilization and obliteration of the infected cavity, and (c) careful attention should be paid to the nutrition of the patient.¹⁰ When those guidelines were followed,

the mortality from streptococcal empyema secondary to influenza fell to 4.3%.⁴⁴ Those guidelines provide the basis for the treatment of parapneumonic effusions today.

NATURAL HISTORY OF PARAPNEUMONIC EFFUSIONS

The evolution of a parapneumonic pleural effusion can be divided into three stages—the exudative, the fibropurulent, and the organization stage.³ The three stages are not sharply defined, but rather form a continuous spectrum. The first stage is the exudative stage, characterized by the rapid outpouring of fluid into the pleural space. The pleural fluid probably originates in the interstitial spaces of the lung.²² In the exudative stage, the pleural fluid is not loculated and is characterized by a low white blood cell count and lactic acid dehydrogenase (LDH) level and a normal glucose level and pH.²³ If appropriate antibiotic therapy is instituted at this time, the pleural effusion does not progress to the fibropurulent stage and tube thoracostomy is not required.²³

The second stage is the fibropurulent stage, characterized by the accumulation of large amounts of pleural fluid with many polymorphonuclear leukocytes, bacteria, and cellular debris. As the stage progresses, the pleural fluid pH and glucose levels become progressively lower and the LDH level progressively higher. The pleural fluid white blood cell count is frequently lower than one would anticipate from looking at the thickness of the fluid; fibrin and cellular debris rather than intact white cells account for the thickness and opacity of the fluid. Fibrin is deposited in a continuous sheet, covering the visceral and parietal pleura. As the stage progresses, there is a tendency toward loculation and the formation of limiting membranes. The loculations contain the infected pleural fluid within compartments, but make drainage of the pleural space increasingly difficult.

The third stage is the organization stage, characterized by the ingrowth of fibroblasts into the thick exudate from the visceral and parietal pleural surfaces to produce an inelastic membrane called the *pleural peel*. The peel prevents the underlying lung from expanding; decortication is required to cure the patient at this stage. In the third stage, the fluid is usually multiloculated and thick. If the patient is not treated, the fluid may drain

spontaneously through the chest wall (*empyema necessitatis*) or into the lung, producing a bronchopleural fistula. If a bronchopleural fistula develops in this situation, immediate drainage of the pus from the pleural space is imperative. Otherwise, the pus from the pleural space will enter the tracheobronchial tree and produce an overwhelming pneumonia.²³

CLASSIFICATION OF PARAPNEUMONIC EFFUSIONS

When a patient with pneumonia is first evaluated, one should attempt to determine whether or not a pleural effusion is present. A lateral radiograph should be obtained to screen for the presence of a pleural effusion. If both diaphragms cannot be seen throughout their entirety on the lateral chest radiograph, decubitus chest radiographs should be obtained. The amount of free-pleural fluid can be semiquantitated by measuring the distance between the inside of the chest wall and the outside of the lung. If that distance (the thickness of the pleural fluid) is greater than 10 mm, thoracentesis should be performed. The only way to determine whether invasive measures are necessary for the treatment of a parapneumonic effusion is to examine the pleural fluid.²⁵ One should perform the thoracentesis as soon as the pleural effusion is recognized because a free-flowing, easily treated parapneumonic effusion can progress to a multiloculated parapneumonic effusion within hours.³⁵

It is important to realize that not all parapneumonic effusions and not all complicated parapneumonic effusions are the same. The classification outlined in Table 1 was developed to assist the practicing physician in the initial care of patients with parapneumonic effusions. It is based on the amount of fluid, the gross and biochemical characteristics of the pleural fluid, and whether or not the pleural fluid is loculated. As one moves down on Table 1, the treatment of the parapneumonic effusion becomes more difficult and increasingly invasive procedures are indicated.²³

When a patient with a parapneumonic effusion more than 10 mm in thickness on the decubitus radiograph is evaluated, one must perform thoracentesis to place the patient in one of the six lower categories. Because it is not known whether an aggressive approach to the pleural fluid collection is indicated until after the pleural fluid has been analyzed,

Table 1. A CLASSIFICATION AND TREATMENT SCHEME FOR PARAPNEUMONIC EFFUSIONS AND EMPYEMA

Class 1	Small
Nonsignificant	< 10 mm thick on decubitus radiograph
Pleural effusion	No thoracentesis indicated
Class 2	> 10 mm thick
Typical parapneumonic	Glucose > 40 mg/dL, pH > 7.2,
Pleural effusion	Gram's stain and culture negative
	Antibiotics alone
Class 3	7.0 < pH < 7.2 or LDH > 1000, and glucose > 40 mg/dL
Borderline complicated	Gram's stain and culture negative
Pleural effusion	Antibiotics plus serial thoracentesis
Class 4	pH < 7.0 or glucose < 40 mg/dL, or Gram's stain or culture positive
Simple complicated	Not loculated, not frank pus
Pleural effusion	Tube thoracostomy plus antibiotics
Class 5	pH < 7.0 or glucose < 40 mg/dL, or Gram's stain or culture positive
Complex complicated	Multiloculated
Pleural effusion	Tube thoracostomy plus thrombolytics
	Thoracoscopy if above ineffective
Class 6	Frank pus present
Simple empyema	Single locule or free flowing
	Tube thoracostomy ± decortication
Class 7	Frank pus present
Complex empyema	Multiple locules
	Tube thoracostomy plus thrombolytics
	Usually require thoracoscopy or decortication

Adapted from Light RW: Pleural Diseases, ed 3, Baltimore, MD, Williams and Wilkins, 1995; with permission.

the question is whether a diagnostic or therapeutic thoracentesis originally should be performed.

I recommend that a therapeutic thoracentesis be performed in all patients whose pleural fluid is more than 10 mm thick on the decubitus view. If there is no reaccumulation of fluid, one need not worry about the parapneumonic effusion. Performance of the therapeutic thoracentesis will also delineate whether the pleural fluid is loculated.

The pleural fluid should be sent for Gram's stain and bacterial culture, white blood cell count and differential, and for determination of its level of glucose, LDH, and pH. If the pH is determined, it must be done with the same care as is an arterial pH level. The fluid should be collected in a heparinized syringe and placed in ice for its transfer to the blood gas laboratory. The pH cannot be determined accurately with a pH meter or tape. If the pH is low (< 7.2) and the glucose is close to 100 mg/dL and there is no large increase in pleu-

ral fluid LDH, one should measure the arterial blood pH before a tube thoracostomy is performed; if systemic acidosis is present, the pleural fluid pH will be acidotic.²⁶ The differential cell count is important because, if polymorphonuclear leukocytes do not predominate, an alternate diagnosis must be sought.

Class 1—Nonsignificant Parapneumonic Effusion

Patients with class 1 parapneumonic effusions have free-flowing fluid that is less than 10 mm thick on the decubitus chest radiograph. Individuals with class 1 effusions should not be subjected to thoracentesis because treatment with appropriate antibiotics almost always resolves the effusion.²⁵ In addition, a thoracentesis is more difficult in patients with a small amount of pleural fluid. If a patient with a Class 1 effusion subsequently develops a larger pleural effusion, a diagnostic thoracentesis should be performed.

Class 2—Typical Parapneumonic Effusion

Patients with a typical parapneumonic effusion have pleural fluid that is free-flowing, with a thickness of greater than 10 mm on the decubitus radiograph. In addition the pleural fluid glucose level is greater than 40 mg/dL, the pleural fluid pH is higher than 7.2, the pleural fluid LDH level is below 1000 U/L, and the bacterial smears and cultures are negative. As a parapneumonic effusion evolves from the exudative stage to the fibropurulent stage, the LDH level becomes progressively higher, whereas the pH and glucose level become progressively lower. When glucose and pH are greater than 40 mg/dL and 7.2, respectively, and the LDH is less than 1000 U/L (or three times the upper normal limit for serum), the effusion is early in the exudative stage and no invasive procedure is necessary.²⁵ If the effusion rapidly recurs after the initial therapeutic thoracentesis or if the patient remains toxic with significant pleural fluid, then a repeat therapeutic thoracentesis should be performed.

Class 3—Borderline Complicated Parapneumonic Effusion

Patients with class 3 parapneumonic effusions have negative bacterial smears and cul-

tures and a glucose level above 40 mg/dL, but the pH is between 7 and 7.2, the LDH level is above 1000 U/L, or the pleural fluid is loculated. The relatively low pH, relatively high LDH, and the loculation all indicate a high level of inflammation in the pleural space. Some class 3 pleural effusions resolve with no invasive procedure but others do not. Our philosophy has always been that we would rather insert a few too many chest tubes than insert some chest tubes too late.

If the patient has an earlier therapeutic thoracentesis that demonstrated the pleural fluid was loculated and the size of the loculated effusion did not decrease with antibiotic treatment or the patient remained toxic, then a small chest tube should be inserted. Thrombolytics can be injected through the small chest tube in an effort to break down the loculations.

If the fluid is not loculated, a repeat therapeutic thoracentesis is indicated if the fluid reaccumulates. If the pleural fluid pH and glucose show a tendency to decrease and the pleural fluid LDH shows a tendency to increase, then a small chest tube should be inserted. If the pleural fluid pH increases above 7.2 and the pleural fluid glucose increases above 40 mg/dL, then resolution is expected and additional therapeutic thoracenteses are not indicated.

Class 4—Simple-Complicated Parapneumonic Effusion

Patients with class 4 parapneumonic effusions have a pleural fluid pH less than 7, a pleural fluid glucose less than 40 mg/dL, and a positive Gram's stain or culture. The pleural fluid does not look like pus and it is not loculated. Patients with class 4 parapneumonic effusions should be treated with some form of invasive therapy because many will not resolve with antibiotic therapy alone.

If the patient's initial thoracentesis was therapeutic, the patient can be managed with either a repeat therapeutic thoracentesis or the placement of a chest tube, should the effusion recur. A reasonable approach is to perform a repeat serial therapeutic thoracentesis if the pH, LDH, and glucose levels in the pleural fluid are improving. Alternatively, if the pH and the glucose levels in the pleural fluid are not improving, then tube thoracostomy should be performed.

If only a diagnostic thoracentesis was per-

formed originally, then the patient should be treated with either a therapeutic thoracentesis or a tube thoracostomy. It appears that such effusions can be managed with relatively small chest tubes (8.3–16F) inserted percutaneously.^{21, 42} The advantage of the smaller tube over a larger one is that its insertion is easier and less painful and its presence is less uncomfortable to the patient.

Class 5—Complex Complicated Parapneumonic Effusion

Patients with class 5 parapneumonic effusion meet the criteria for class 4 parapneumonic effusions but the fluid is also loculated. Such patients should be treated with a small chest tube plus intrapleural-thrombolytic agents. Without the thrombolytic therapy, the pleural space cannot be drained completely. If complete drainage of the pleural space is not accomplished after one or two doses of thrombolytic therapy, then more aggressive therapy, such as the breakdown of the loculations with thoracoscopy or thoracotomy with decortication, should be performed.

Class 6—Simple Empyema

Patients with class 6 parapneumonic effusions have pleural fluid that is frank pus and the pus is either free-flowing or confined to a single loculus. Such patients should be treated with a relatively large (~28–36F) chest tube because the thick pus is likely to obstruct a smaller one. Patients who have class 6 parapneumonic effusions frequently have a thick peel over the visceral pleura that prevents the underlying lung from expanding. If a sizable empyema cavity remains after several days of chest tube drainage, consideration should be given to performing a decortication to eradicate the empyema cavity.

Class 7—Complex Empyema

Patients with class 7 parapneumonic effusions have frank pus in their pleural space that is multiloculated. Although such patients initially should be treated with large chest tubes and intrapleural thrombolytic agents, more invasive measures such as thoracoscopy with the breakdown of adhesions or thoracot-

omy with decortication are necessary in the majority.⁴³ If the drainage of the pleural space is unsatisfactory or a large empyema cavity remains after several days, either thoracoscopy or thoracotomy should be considered.

TREATMENT MODALITIES FOR PARAPNEUMONIC EFFUSIONS

Antibiotic Therapy

Patients with pneumonia and pleural effusion should be treated with antibiotic agents. The initial antibiotic selection is based on whether the pneumonia is community- or hospital-acquired and on the severity of illness. The initial antibiotic selection and the dose are not influenced by the presence or absence of a pleural effusion. Most antibiotic agents are present in pleural fluid at levels that are comparable with those in serum.²³ Aminoglycosides, however, appear to penetrate poorly into purulent pleural fluid.⁵⁰

Hospitalized patients with community-acquired pneumonias that are not severe should be treated with second- or third-generation cephalosporins or a β -lactam/ β -lactamase inhibitor. If infection with *Legionella* spp is likely, a macrolide antibiotic agent should be added. Patients with severe community-acquired pneumonia should be treated with a macrolide plus a third-generation cephalosporin such as ceftazidime or cefoperazone. Patients with hospital-acquired pneumonia should be treated with a third-generation cephalosporin with anti-*Pseudomonas* activity. If *Staphylococcus aureus* infection is suspected, either nafcillin or vancomycin should be administered.³²

Therapeutic Thoracentesis

Therapeutic thoracentesis was first proposed as treatment for parapneumonic effusions in the middle of the nineteenth century.^{8, 51} In 1962, the American Thoracic Society recommended repeated thoracenteses for nontuberculous empyemas in the early exudative phase.³ Recently, however, therapeutic thoracentesis has received relatively little attention as a treatment for parapneumonic effusions.

Therapeutic thoracentesis is the least invasive of the invasive treatment modalities for parapneumonic effusions. As discussed ear-

lier, a logical approach to patients with parapneumonic effusions is to do a therapeutic thoracentesis when the effusion is first recognized. If the fluid subsequently recurs, a second therapeutic thoracentesis should be performed. If the pleural fluid again recurs and the pleural fluid biochemical parameters were worsening at the time of the second thoracentesis, a chest tube should be inserted.

A few recent studies suggested there is a role for therapeutic thoracentesis in the management of patients with parapneumonic effusions. Sasse and coworkers³⁶ reported that therapeutic thoracentesis was at least as good as chest tube placement in the treatment of early pleural infections in a rabbit model of empyema. Storm and coworkers⁴⁴ reported that 48 of 51 patients (94%) with empyema (purulent pleural fluid or positive microbiologic studies on the pleural fluid) were treated successfully with daily thoracentesis. Mandal and associates²⁸ reported that 28 of 111 patients (25%) with bacterial empyema (purulent exudate or positive culture) were treated successfully with serial therapeutic thoracentesis and antibiotic agents. Ferguson et al¹² reported that 19 of 46 patients (41%) with empyema (opaque fluid in the pleural space with the cloudiness attributable to neutrophils or organisms) were treated successfully with repeated thoracentesis.

There have been no controlled studies comparing therapeutic thoracentesis with small tube thoracostomy in the treatment of patients with class 3 or class 4 parapneumonic effusion.

Tube Thoracostomy

When a chest tube is used to treat a parapneumonic effusion, it should be placed in a dependent part of the effusion. Failure of tube thoracostomy in the treatment of parapneumonic effusions is frequently attributable to placing the tube in the wrong position.²¹ Initially, the chest tube should be connected to an underwater-seal drainage system with suction. If the visceral pleura is covered with a fibrinous peel, the application of negative pressure may facilitate the expansion of the underlying lung and hasten obliteration of the empyema cavity.

In the past, it was recommended that relatively large (26–36F) chest tubes be used in the treatment of parapneumonic effusions based on the belief that smaller tubes would

become obstructed with the fluid. It appears, however, that class 3, 4, and 5 parapneumonic effusions can be managed with smaller tubes. Forty-one of 53 patients (77%) in two recent series were managed successfully with smaller chest tubes (8.3–16F).^{21, 42} Those results are at least as good as those reported in recent series in which larger tubes were used.^{2–4} The small chest tubes in the two series^{21, 42} were inserted percutaneously by an interventional radiologist. It is likely that the excellent results are related to accurate placement of the catheter. If the pleural fluid is frank pus, we still prefer to use a large chest tube.

Successful closed-tube drainage of complicated parapneumonic effusions is evidenced by improvement in the clinical and radiologic status within 24 hours. If the status of the effusion is not clear from the posteroanterior and lateral radiograph, chest CT scan can provide valuable information. If the patient is not improving, either the drainage is inadequate or the patient is receiving the wrong antibiotic agent. Inadequate drainage can be caused by poor positioning of the chest tube, obstruction of the chest tube, or loculated pleural fluid. If the drainage is incomplete because of loculations, thrombolytic agents can be administered intrapleurally or the patient can be subjected to thoracoscopy, with the breakdown of the loculations.

If the patient responds satisfactorily, how long should the chest tube be left in place? Although there has been surprisingly little written on the subject, we recommend that the chest tubes should be left in place until the volume of the pleural drainage is under 50 mL 24 hours and until the draining fluid becomes clear yellow.²³ If the chest tube ceases to function (no fluctuation with respiratory efforts), it should be removed because it serves no useful purpose and can be a conduit for pleural suprainfection. On occasion, purulent drainage continues from the chest tube despite improvement clinically and radiologically. In that situation, one must decide whether a more aggressive approach—e.g., decortication—is indicated. That decision can be aided by radiographs obtained after the injection of contrast material into the pleural space through the chest tube.⁴⁰ If only a tube tract is demonstrated, the chest tube can be withdrawn over several days while the tract is allowed to fill in with granulation tissue. When a larger (>100 mL) cavity is demonstrated, consideration should be given

to performing an empyemectomy. If one elects to continue with chest tube drainage, progress of the empyema cavity can be assessed by repeated contrast studies through the tube at weekly intervals.

Intrapleural Thrombolytic Therapy

The role of thrombolytic agents in the management of loculated-parapneumonic effusions remains to be determined. The theory behind their use is that loculations in the pleural space are produced by fibrin membranes; if a thrombolytic agent is injected into the pleural space, then it may dissolve the fibrin membranes and facilitate drainage of the pleural space.

In the past 3 years, there have been at least five *uncontrolled* studies,^{7, 20, 22, 30, 48} each with more than 20 patients, that have concluded that thrombolytic agents are useful in the management of patients with loculated pleural effusions. Both streptokinase^{7, 20, 22, 48} and urokinase^{7, 30, 48} have been used in that situation. In several reports, the basis for the endorsement of the intrapleural thrombolytics was the increase in pleural fluid drainage after their administration.

One report compared the efficacy of the two thrombolytic agents and concluded that both were useful adjuncts in the management of complicated parapneumonic effusions, but that urokinase was the thrombolytic agent of choice because there is a greater chance of dangerous allergic reactions to streptokinase.⁷

Each agent can be given daily in a total volume of 50 to 100 mL as long as they appear to be facilitating pleural drainage. The usual dose of urokinase is 100,000 U, that for streptokinase is 250,000 U.

Two placebo-controlled studies evaluated thrombolytic agents in the management of patients with complicated parapneumonic effusion and they reached different conclusions. In the first study, streptokinase, 250,000 U daily, was compared with no thrombolytic agent in the management of 52 patients with loculated parapneumonic effusion.⁹ The study⁹ showed that there was more pleural fluid drainage in patients who received streptokinase, but the duration of hospitalization, the need for more invasive surgery, and the mortality rate in the two groups did not differ significantly.⁹ In the second study, as yet reported only in abstract form, 128 patients were randomized to receive 50,000 U uroki-

nase, 250,000 U streptokinase, or saline lavage daily. The groups that received the thrombolytic agents had significantly greater radiologic improvement and significantly less need for decortication.⁷

Animal studies of thrombolytic agents have not been definitive. Strange and coworkers⁴⁶ showed in one model of experimental empyema that the intrapleural administration of streptokinase increases the amount of pleural fluid but does not decrease the number of adhesions. In a recent study, we demonstrated that, when empyema fluid is incubated with either streptokinase or urokinase, the fluid does not become more liquid. When the empyema fluid is incubated with Varidase, a combination of streptokinase and streptodornase (streptococcal DNAase), however, it becomes completely liquified.³⁷

Given the aforementioned conflicting sets of data, what should be the role of thrombolytics in the management of loculated parapneumonic effusions? When one wishes to drain a loculated parapneumonic effusion, a trial of thrombolytic therapy should be tried if there are no contraindications to their use. If the patient improves clinically and radiologically (not just an increase in the amount of pleural-fluid drainage); so much the better. If there is no such improvement after one or two doses, however, the therapy should be abandoned and more invasive measures taken.

Thoracoscopy

Thoracoscopy, with the breakdown of adhesion, is the procedure of choice when tube thoracostomy plus intrapleural thrombolytic therapy fails. With the advent of video-assisted thoracic surgery, video-thoracoscopy is being used increasingly in the situation under discussion. Several papers (reporting uncontrolled studies) in the past few years demonstrated the use of thoracoscopy in the management of complicated parapneumonic effusions.^{19, 27, 39, 47} One advantage of the procedure is that the chest tube can be positioned in the most dependent part of the empyema cavity.

All patients who have incomplete drainage of their pleural space with chest tubes plus thrombolytic therapy should be considered to be candidates for thoracoscopy. If thorough debridement and complete lung expansion are achieved with thoracoscopy, chest tubes

usually can be removed in 3 to 5 days.⁴⁰ It should be noted, however, that decortication is best done with a full thoracotomy rather than thoracoscopy. It has been recommended that a chest CT scan be obtained prior to thoracoscopy.⁴¹ That examination provides anatomic information about the size and extent of the empyema cavity that guides the planned procedure. A thickened visceral-pleural peel without septations suggests that the empyema may be chronic and probably will not be amenable to thoracoscopic debridement alone.⁴¹

Thoracotomy with Decortication

With this procedure, which involves a full thoracotomy, all the fibrous tissue is removed from the visceral pleura and all pus is evacuated from the pleural space. Decortication eliminates the pleural sepsis and allows the underlying lung to expand. It is a major thoracic operation requiring a full thoracotomy incision and therefore should not be performed on patients who are markedly debilitated.

Decortication is the procedure of choice in a patient whose pleural sepsis is not controlled by the less invasive measures of tube thoracostomy, intrapleural-thrombolytic agents, and thoracoscopy with the breakdown of adhesions. Decortication should be done as soon as it is recognized that the less invasive therapies are ineffective.^{18, 29, 49} In the acute states of a parapneumonic effusion, decortication should be performed only for the control of pleural sepsis, not for pleural thickening. The pleural thickening usually resolves spontaneously over a period of several months.³¹ If after 6 months, the pleura remains thickened and the patient's pulmonary function is reduced sufficiently to limit his activities, decortication should be considered.

Open Drainage Procedures

An open drainage procedure is an alternative to decortication in patients who are too debilitated to undergo decortication. Segments of one to three ribs overlying the lower part of the empyema are resected and one or more short, large-bore tubes are inserted into the empyema cavity. The empyema space must be irrigated daily with a mildly antiseptic solution and the drainage can be collected

in a colostomy bag. The open-drainage procedure must not be performed unless there is fusion of the visceral and parietal pleura throughout most of the pleural space. If such fusion is not present, the lung will collapse. Performance of the open-drainage procedure too early led to the high mortality from parapneumonic effusions experienced during World War I (discussed earlier).

The advantages of open drainage over closed-tube drainage is that the drainage is more complete and the patient is freed from attachment to a closed-drainage system. When the procedure is undertaken, however, one must realize that the median time for complete healing of the wound after an open-drainage procedure is generally lengthy—about 6 months.

SUMMARY

When a patient with a parapneumonic pleural effusion is first evaluated, a therapeutic thoracentesis should be performed if more than a minimal amount of pleural fluid is present. Fluid obtained at the therapeutic thoracentesis should be gram-stained and cultured and analyzed for glucose, pH, LDH, white blood cells, and differential cell count. If the fluid cannot be drained because of loculations, a chest tube should be inserted and thrombolytic agents administered. If the pleural fluid recurs after the initial therapeutic thoracentesis but the patient is doing well clinically and the initial pleural fluid glucose was greater than 60 mg/dL; the pH, greater than 7.2; the LDH, less than three times the upper normal limit for serum and the cultures are negative; he or she can be observed. If one or more of the aforementioned criteria are not met, a second therapeutic thoracentesis should be performed, with repeat diagnostic evaluations of the pleural fluid. If the fluid recurs a second time, a small chest tube should be placed if the pleural fluid glucose and pH were lower and the LDH higher on the second thoracentesis than on the first thoracentesis.

Patients with loculated-parapneumonic effusions should be treated with tube thoracostomy and thrombolytic agents. If drainage is incomplete, thoracoscopy, with breakdown of adhesions and debridement of the pleural space, is indicated. If thoracoscopy is unsuccessful, then thoracotomy, with decortication,

is indicated unless the patient is too debilitated.

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AMERICAN COLLEGE OF CHEST PHYSICIANS

Medical and Surgical Treatment of Parapneumonic Effusions: An Evidence-Based Guideline

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See the complete guideline, "Medical and Surgical Treatment of Parapneumonic Effusions" (CHEST 2000; 118: 1158-1171), for a detailed discussion of the guideline summarized in this Quick Reference Guide and for a complete list of references. The CHEST article and summary of these guidelines and interactive algorithms are available on the Internet at www.chestnet.org.



Purposes

The purposes of the guideline are to (1) establish evidence-based criteria for evaluating the risk for poor outcome in patients with parapneumonic effusions (PPE) complicating bacterial pneumonia, and (2) make evidence-based recommendations for managing PPE in patients with a confirmed diagnosis of bacterial pneumonia.

Excluded from the guideline are PPE complicating trauma, postoperative PPE, pre-existing PPE, and chylous pleural effusions.

Background

Parapneumonic effusions develop in up to 57% of patients hospitalized with bacterial pneumonia. Some PPE resolve with antibiotic treatment of the pneumonia and no specific PPE therapy. In other instances, PPE must be drained in order for the patient to recover.

Clinical approaches vary for choosing (1) which PPE should be drained, and (2) appropriate methods for draining a PPE. Most relevant published literature in the period 1966 to 1998 reports case series in which patient selection and treatment biases may or may not have been present. Three randomized, controlled trials were conducted and reported in the 1966 to 1998 period, with fewer than 100 patients. All relevant literature was critically reviewed.

Pooled data from literature selected for review on the basis of rigorous methodology guidelines, and results of the randomized, controlled trials and historically controlled series revealed consistent, and possibly, clinically meaningful trends in primary management approaches to PPE complicating bacterial pneumonia. Based on trends identified in critically reviewed literature, and on consensus opinion, recommendations were developed for evaluating and managing PPE complicating bacterial pneumonia.

Evaluation of Patients With PPE by Risk for Poor Outcome

Management options for the patient with PPE complicating bacterial pneumonia should be based on risk for poor outcome, *ie*, without adequate drainage of the pleural space, the patient is likely to have any or all of the following:

- prolonged hospitalization
- prolonged evidence of systemic toxicity
- increased morbidity from any drainage procedure
- increased risk for residual ventilatory impairment
- increased risk for local spread of the inflammatory reaction
- increased risk for death

An annotated risk table evaluates the risk for poor outcome in patients with PPE based on three variables:

1. pleural space anatomy
2. pleural fluid bacteriology
3. pleural fluid chemistry

Table 1. Categorizing Risk for Poor Outcome in Patients With PPE

Pleural Space Anatomy	Pleural Fluid Bacteriology	Pleural Fluid Chemistry	Category	Risk of Poor Outcome	Drainage
A ₀ minimal, free-flowing effusion (< 10 mm on lateral decubitus) ¹	AND B _X culture and Gram stain results unknown	AND C _X pH unknown	1	Very low	No ²
A ₁ small to moderate free-flowing effusion (> 10 mm and < 1/2 hemithorax)	AND B ₀ negative culture and Gram stain ³	AND C ₀ pH 7.20	2	Low	No ²
A ₂ large, free-flowing effusion (1/2 hemithorax) ⁴ or loculated effusion, ⁵ or effusion with thickened parietal pleura ⁶	OR B ₁ positive culture or Gram stain	OR C ₁ pH < 7.20	3	Moderate	Yes
	B ₂ pos PUS		4	High	Yes

¹ pH is the preferred pleural fluid chemistry test⁷ and pH must be determined using a blood gas analyzer.^{8,9} If a blood gas analyzer is not available, pleural fluid glucose should be used (P₀ glucose 60 mg/dL, P₁ glucose < 60 mg/dL). The panel cautions that the clinical utility and decision thresholds for pH and glucose have not been well-established.

² Clinical experience indicates that effusions of this size do not require thoracentesis for evaluation, but will resolve.⁷

³ If thoracentesis were performed in a patient with A₀ category pleural anatomy and P₁ or B₁ status found, clinical experience suggests that the P₁ or B₁ findings might be a false-positive. Repeat thoracentesis should be considered if effusion enlarges and/or clinical condition deteriorates.

⁴ Regardless of prior use of antibiotics.

⁵ If clinical condition deteriorates, repeat thoracentesis and drainage should be considered.

⁶ Larger effusions are more resistant to effective drainage, possibly because of the increased likelihood that large effusions will also be loculated.¹⁰

⁷ Pleural loculations suggest a worse prognosis.¹¹

⁸ Thickened parietal pleura on contrast-enhanced CT suggests presence of empyema.^{12,13,14}

Primary Management Approaches

Primary approaches are those performed first to manage a PPE. This is in contradistinction to a rescue approach, an approach performed after an earlier attempt at management failed. Primary management approaches include the following:

- No drainage
- Therapeutic thoracentesis
- Tube thoracostomy
- Fibrinolytic therapy (requires tube thoracostomy to administer drug)
- Video-assisted thorascopic surgery (VATS) (includes postprocedure tube thoracostomy)
- Surgery, including thoracostomy and rib resection

Management Recommendations

The presence of PPE should be considered in all patients with a confirmed diagnosis of acute bacterial pneumonia.

In patients with confirmed PPE, estimated risk for poor outcome (Table 1) should be the basis for determining whether a PPE should be drained.

Category I and II PPE for Poor Outcome

Patients with category I and II PPE may not require drainage.

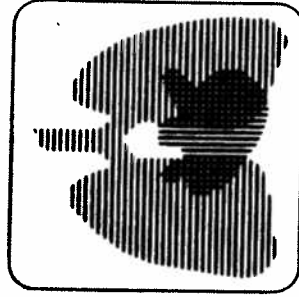
Category III and IV PPE for Poor Outcome

Drainage is recommended for management of category III and IV PPE, based on pooled data for mortality and the need for a second intervention if no drainage is performed.

Therapeutic thoracentesis or tube thoracostomy alone appears to be insufficient treatment for managing most category III and IV PPE. However, in the individual patient, these modalities may be planned in interim steps to complete drainage. Occasionally, they may result in complete resolution of the PPE before drainage is performed. Careful evaluation of the patient over hours is then necessary; if resolution is complete, no further intervention is necessary.

Fibrinolysis (streptokinase, urokinase), VATS, and surgery are acceptable approaches for managing category III and IV PPE. This recommendation is based on cumulative data across all studies that indicate that these interventions are associated with the lowest mortality and need for second interventions.

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