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Parapneumonic Pleural Effusions and Empyema Thoracis

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Updated: Sep 17, 2009

Introduction

Background

Pleural effusions are a common finding in patients with pneumonia. More than 40% of patients with bacterial pneumonia and 60% of patients with pneumococcal pneumonia develop parapneumonic effusions. While treatment with antibiotics leads to resolution in most patients, some patients develop a more fibrinous reaction, with the presence of frank pus in the most severe cases. The latter is referred to as an empyema or empyema thoracis.

Parapneumonic pleural effusions are classified into 3 broad groups based on fluid characteristics, which, in turn, provides a reflection on both the severity and natural history of the pleural effusion.

- Uncomplicated parapneumonic effusions: These are exudative, predominantly neutrophilic effusions reflecting increasing passage of interstitial fluid as a result of inflammation associated with pneumonia. The fluid may be slightly cloudy or even clear, without any organisms noted on Gram stain or culture. They resolve with appropriate antibiotic treatment of the pneumonia.
- Complicated parapneumonic effusions: These occur as a result of bacterial invasion into the pleural space that leads to an increased number of neutrophils, decreased glucose levels, pleural fluid acidosis, and an elevated lactic dehydrogenase (LDH) concentration. These effusions often are sterile because bacteria are usually cleared rapidly from the pleural space. The fluid is typically cloudy and is classified as complicated because it requires drainage for resolution.
- Empyema thoracis: This develops as frank pus accumulates in the pleural space. Laboratory studies indicate that preexisting pleural fluid is required for the development of an empyema because empyema is not seen after direct inoculation into a "dry" pleural space. The pus is seen after thoracentesis or any drainage procedure of the pleural space and is generally characterized as thick, viscous, and opaque.

Empyema thoracis has been recognized as a serious problem for centuries. In approximately 500 BCE, Hippocrates recommended treating empyema with open drainage. The treatment of empyema remained essentially unchanged until the middle of the 19th century. In 1876, Hewitt described a method of closed drainage of the chest in which a rubber tube was placed into the empyema cavity to drain via a water seal drainage method. In the early 20th century, surgical therapies for empyema (eg, thoracoplasty, decortication) were introduced. More recently, video-assisted thoracoscopic surgery (VATS) has played a major role in the treatment of patients with empyema thoracis.

Etiology

Virtually any type of pneumonia (eg, bacterial, viral, atypical) can be associated with parapneumonic pleural effusions. However, the relative incidence of parapneumonic pleural effusions varies with the organism. Viral pneumonia and *Mycoplasma* pneumonia cause small pleural effusions in 20% of patients. For thoracic empyema, bacterial pneumonia is the cause in 70%[1]. Increasingly, empyema thoracis is a complication of previous surgery, which accounts for 30% of cases. Trauma may also be complicated by superinfection of the pleural space. In the absence of trauma or surgery, the infecting organism may spread from blood or other organs into the pleural space. These can

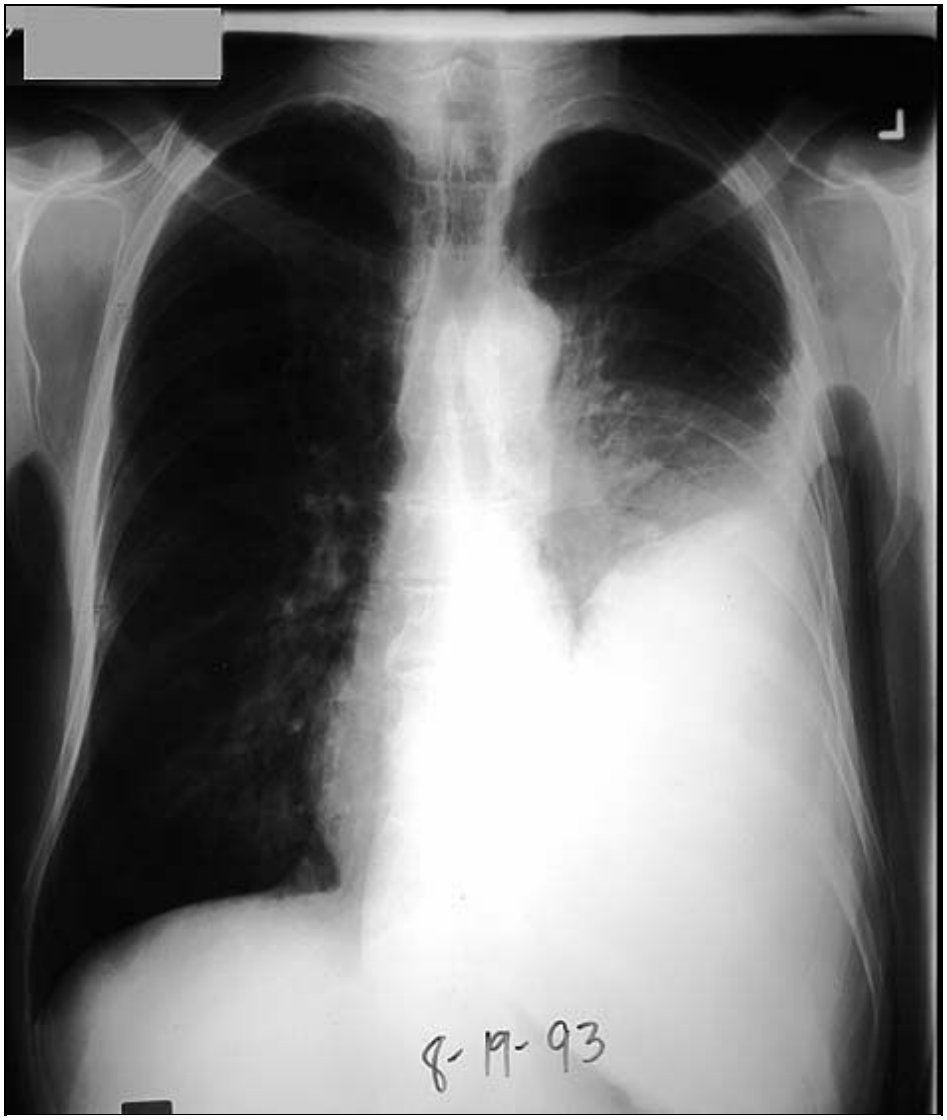
develop into subdiaphragmatic abscesses, a ruptured esophagus, mediastinitis, osteomyelitis, pericarditis, cholangitis, and diverticulitis, among others.

Bacteriology

Bacteriologic features of culture-positive parapneumonic pleural effusions have changed over time. Prior to the antibiotic era, *Streptococcus pneumoniae* was the most common. *S pneumoniae* and *Staphylococcus aureus* account for approximately 70% of aerobic gram-positive cultures. Presently, aerobic organisms are isolated slightly more frequently than anaerobic organisms. *Streptococcus milleri* has also become more common.[2,3,4] *Klebsiella, Pseudomonas,* and *Haemophilus* species are the 3 most commonly isolated aerobic gram-negative organisms. *Bacteroides* and *Peptostreptococcus* species are the 2 most commonly isolated anaerobic organisms. Currently, empyema thoracis is most often associated with aspiration pneumonia with mixed bacterial florae containing aerobic and anaerobic bacteria.[5] The usual organism isolated in empyema thoracis complicating previous surgery is *S aureus*.

Pathophysiology

The evolution of a parapneumonic pleural effusion, as shown in the image below, can be divided into 3 stages, including exudative, fibrinopurulent, and organization stages.[1]



Left pleural effusion developed 4 days after antibiotic treatment for pneumococcal pneumonia. Patient developed fever, left-sided chest pain, and increasing dyspnea. During thoracentesis, purulent pleural fluid was removed, and the Gram stain showed gram-positive diplococci. The culture confirmed this to

be Streptococcus pneumoniae.

During the exudative stage, sterile pleural fluid rapidly accumulates in the pleural space. The pleural fluid originates in the interstitial spaces of the lung and in the capillaries of the visceral pleura because of increased permeability. The pleural fluid has a low WBC count and LDH level, and the glucose and pH levels are within the reference range. These effusions resolve with antibiotic therapy, and chest tube insertion is not required. This stage takes approximately 2-5 days from the onset of pneumonia.

In the second stage, or fibrinopurulent stage, bacterial invasion of the pleural space occurs, with accumulation of polymorphonuclear leukocytes, bacteria, and cellular debris. A tendency toward loculation and septation exists, pleural fluid pH (<7.20) and glucose levels are lower (<60 mg/dL), and the LDH level increases. At this stage, bacteriological stains and/or cultures of the pleural fluid can be positive for microorganisms. This stage takes approximately 5-10 days after pneumonia onset.

In the last, or organization stage, fibroblasts grow into the exudates from both the visceral and parietal pleural surfaces, and they produce an inelastic membrane called pleural peel. Pleural fluid is thick. In an untreated patient, pleural fluid may drain spontaneously through the chest wall (ie, empyema thoracis necessitatis). Empyema thoracis may arise without an associated pneumonic process, such as from esophageal perforation, trauma, a surgical procedure on pleural space, or septicemia. This last stage may take 2-3 weeks to develop.

Frequency

United States

Based on hospital discharge data, approximately 1.3 million patients are hospitalized each year with pneumonia in the United States. The prevalence of parapneumonic effusions is dependent, in part, on the organism involved. Overall, pleural effusions are seen in approximately 35-40% of patients with bacterial pneumonia or anaerobic pneumonia, with a prevalence in pneumococcal pneumonia approaching 60%. Complicated pleural effusions are more commonly seen with anaerobic pleuropulmonary infections. This results in an estimated 500,000-750,000 patients with parapneumonic effusions annually. No good estimates are available regarding the fraction of these patients that proceed to complicated effusions or empyema, but in small series, a reported approximately 5-10% require a drainage or a surgical procedure.

International

No good estimates are available on the international incidence of pneumonia. The World Health Organization has reported the burden of disease related to deaths from lower respiratory tract infections in 2004 at 4.2 million. One can extrapolate the incidence of pleural effusions and empyema using a US estimate, but caution is advised because the lack of treatment and delayed treatment skew the international incidence upward.

Risk factors

Risk factors for empyema thoracis include age (children and elderly persons), debilitation, pneumonia requiring hospitalization, and comorbid diseases, such as bronchiectasis, rheumatoid arthritis, alcoholism, diabetes, and gastroesophageal reflux disease.[1]

A large prospective observational study in the United Kingdom, using multivariate regression analysis, identified 7 clinical factors predicting the development of complicated parapneumonic pleural effusions or empyema thoracis. They identified an albumin value of less than 30 g/L, a serum sodium value of less than 130 mmol/L, a platelet count of greater than 400 X 10^9/L, a C-reactive protein level of greater than 100 mg/L, and a history of alcohol abuse or intravenous drug use as independently associated with the development of complicated parapneumonic pleural effusions or empyema thoracis, while a history of chronic obstructive pulmonary disease (COPD) was associated with a decreased risk.[6]

Mortality/Morbidity

Mortality rates from empyema have been reported to be 11-50% range. The wide difference is due in part to limited data, with mortality rates being higher (in the 50% range) at a time when current diagnostic imaging, antibiotics, and drainage options were not readily available. Other complicating factors include cardiac and respiratory comorbidities, immunosuppressive states related to medications or HIV infection, and age. Death rates related to pneumonia are higher in elderly persons and in those with the outlined underlying comorbidities. More recent reports estimate deaths in patients with pneumonia and complicated pleural effusions in the 7-10% range.

Race

No specific ethnic predisposition is recognized for empyema; however, a larger number of ethnic minorities have limited financial resources, limited access to healthcare, and more comorbidities, which, in turn, may increase their risk of pneumonia, pleural effusions, and empyema.

Sex

Empyema has no known sexual predilection.

Age

No specific age predisposition is recognized for empyema, although increasing age and associated comorbidities increase the risk for pneumonia and, subsequently, pleural effusions and empyema. Also recognized is that differences exist in empyema that occurs in children compared with adults. The most striking differences include the development of empyema in previously healthy children (as opposed to adults who usually have some underlying comorbidity) and the lower threshold for treatment with thrombolytics and surgical drainage in children compared with adults. See Empyema for more details.

Clinical

History

Clinical manifestations of parapneumonic effusions and empyema largely depend on whether the patient has an aerobic or anaerobic infection. Aerobic infections are more acute in onset with acute febrile symptoms, while anaerobic infections can be indolent in their time course and symptoms may be nonspecific with low-grade fevers. If fever persists for more than 48 hours after the initiation of antibiotic treatment, a complicating parapneumonic effusion or empyema likely exists.

- Aerobic bacterial pneumonia
  - The clinical presentation in patients with aerobic bacterial pneumonia is similar to that of patients with bacterial pneumonia.
  - Patients present with an acute febrile illness with chest pain, sputum production, and leukocytosis.
  - A complicated parapneumonic effusion is suggested by the presence of a fever lasting more than 48 hours after the initiation of antibiotic therapy.
- Anaerobic bacterial infection
  - Patients with anaerobic bacterial infections involving the pleural space usually present with a subacute illness.
  - Most of these patients have symptoms persisting for more than 7 days.
  - Approximately 60% of patients have weight loss.
  - Anemia is also common.
  - Most of these patients have poor oral hygiene, many have alcoholism, and others have factors that predispose them to recurrent aspiration.

Physical

Most patients are febrile with tachypnea and tachycardia, often appearing toxic and fulfilling criteria for the systemic

inflammatory response syndrome (SIRS). Signs of pleural effusion upon physical examination include the following:

- Decreased or absent breath sounds
- Dullness to percussion
- Decreased tactile fremitus
- Evidence of tension and contralateral tracheal shift possible with large effusions

In areas in which pneumonia and lung consolidation are adjacent and more extensive than pleural fluid, findings include (1) rales or crackles and/or (2) bronchial breath sounds or egophony.

Causes

See Background for details on the etiology and bacteriology of these pleural infections.

- Pneumonia is the leading cause of parapneumonic effusions and empyema thoracis.
- Increasingly, empyema is also a complication of previous cardiothoracic surgery, which accounts for 30% of cases. The usual organisms are *Staphylococcus* species and gram-negative bacteria.
- Trauma can also lead to inoculation and superinfection of the pleural space.
- In the absence of trauma or surgery, the infecting organism may have spread from blood or other organs into the pleural space. These causes include extension of infections from adjacent or distant sites (eg, ruptured esophagus, mediastinitis, osteomyelitis, pericarditis, cholangitis, diverticulitis, pericarditis) or subdiaphragmatic abscesses.

Differential Diagnoses

Boerhaave Syndrome
Hemothorax
Intra-abdominal Sepsis
Lung Abscess
Lung Cancer, Non-Small Cell
Lung Cancer, Oat Cell (Small Cell)
Pleural Effusion
Pleurodynia
Pneumococcal Infections
Pneumonia, Aspiration
Pneumonia, Bacterial
Pneumonia, Community-Acquired
Pneumonia, Fungal
Secondary Lung Tumors
Tuberculosis

Other Problems to Be Considered

Malignant pleural effusion
Tuberculous pleural effusion
Esophageal perforation (Boerhaave syndrome)
Drug-induced pleural effusion
Pleuritis secondary to systemic collagen-vascular diseases
Subdiaphragmatic abscess

Workup

Laboratory Studies

So specific laboratory studies suggest the presence of a parapneumonic effusion or empyema. However, the

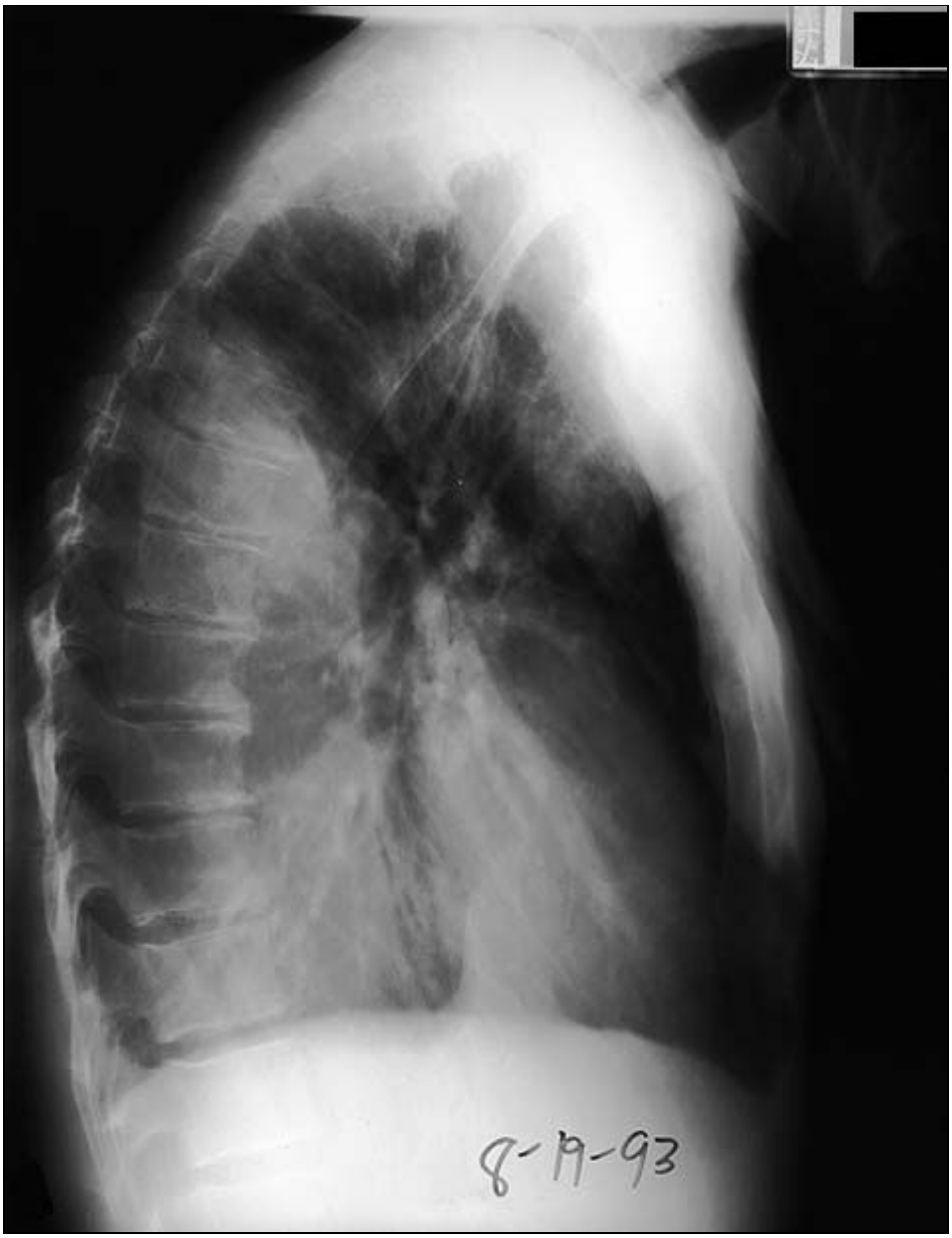
possibility of a parapneumonic effusion and empyema should be a consideration for every patient with pneumonia. The presence of pleural fluid may be suggested based on physical examination findings; however, small pleural effusions may not be detected during the physical examination. In this case, any significant effusion can be visualized using 2-view (ie, posteroanterior, lateral) chest radiography.

Sputum should be submitted for culture, especially if purulent. The infecting organism may be suggested based on Gram stain results. Mixed florae are often seen in anaerobic infections.

As with any infection, leukocytosis may be present (>12,000/µL); however, it should decrease with adequate antibiotic therapy. Persistent fever and leukocytosis despite adequate antibiotic therapy may signal a persistent focus of infection, such as a complicated parapneumonic effusion or empyema, with subsequent evaluation as outlined in the following sections. Diagnosing a complicated parapneumonic effusion and/or empyema is crucial for optimal management because a delay in drainage of the pleural fluid substantially increases morbidity.

Imaging Studies

- Chest radiography
  - Lateral chest radiography usually demonstrates the presence of a significant amount of pleural fluid, as shown in the image below.
  -



Left lateral chest radiograph shows a large, left pleural effusion.

- If either of the diaphragms is not visible throughout its entire length, the posterior costophrenic angles are blunted, or a lateral meniscus is visible, obtain bilateral decubitus chest radiographs.
- Free pleural fluid is seen as a dense linear shadow layering between the chest wall and the lung parenchyma.
- Unchanging pleural-based linear densities, pleural-based masslike densities, or collections with obtuse angles suggest the presence of loculated fluid, especially if the differences in the fluid or the appearance between upright and lateral views are minimal.
- If the pleural fluid distance measures more than 10 mm from the chest wall, sufficient fluid is present to perform a diagnostic thoracentesis.

- Ultrasonography
  - Ultrasonography can be used to localize fluid for a thoracentesis. Fluid appears dark or black on ultrasound images, and most bedside ultrasonography devices permit measurement of the depth of location from the chest wall.
  - Complex fluid (purulent or viscous) may have more density or shadows within in the pleural fluid collection. Sometimes, fibrinous strands can be seen floating in the pleural fluid.
  - Other structures such as the diaphragm or lung parenchyma can provide landmarks to assist in needle placement for thoracentesis.
  - Loculated pleural effusions may be difficult to localize during physical examination, but they can usually be identified with ultrasonography.
  - Ultrasonography can effectively distinguish loculated pleural fluid from an infiltrate. The latter may have air bronchograms visible, but the distinction may be difficult if dense consolidation is present. If a loculated pleural effusion is suspected, an ultrasonographic examination is recommended for diagnosis and marking the area for thoracentesis.

- CT scanning of the thorax
  - CT scanning of the chest with contrast, as shown in the image below, enhances the pleural surface and assists in delineating the pleural fluid loculations.
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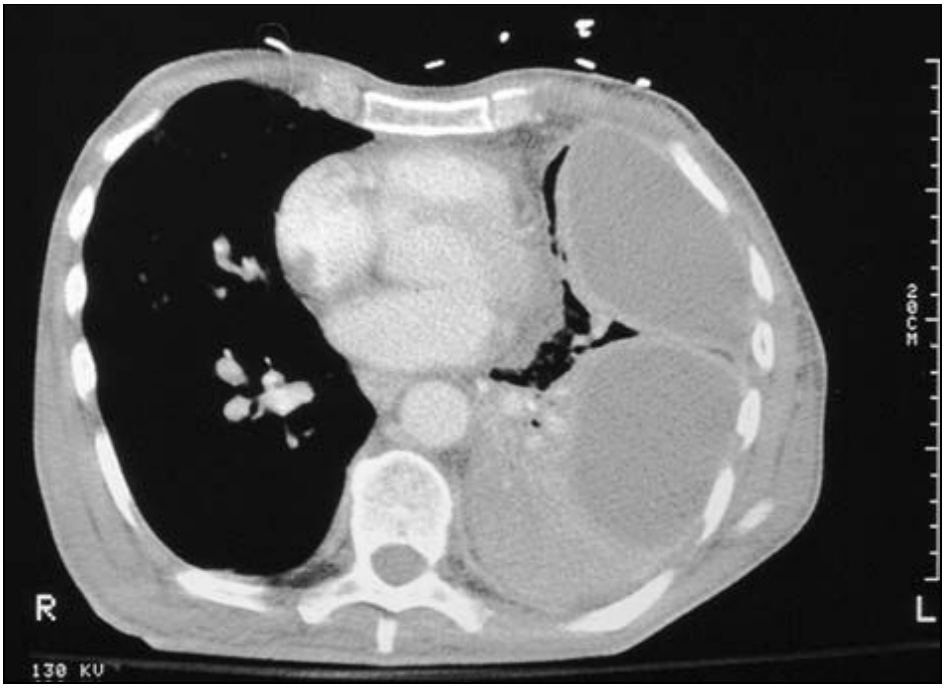
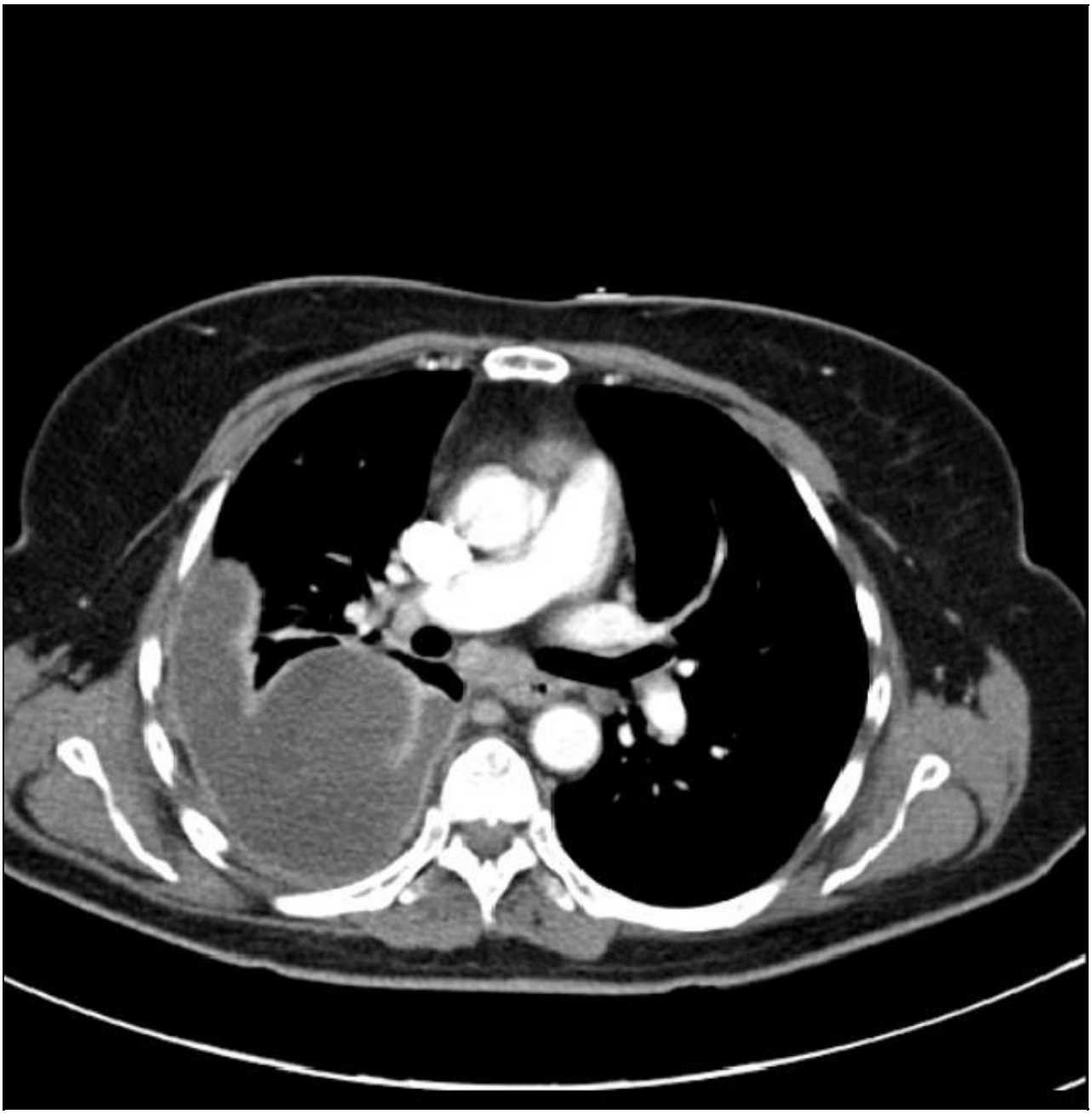


CT scan of thorax shows loculated pleural effusion on left and contrast enhancement of visceral pleura, indicating the etiology is likely an empyema.



Chest CT scan with intravenous contrast in a patient with mixed Streptococcus milleri and anaerobic empyema following aspiration pneumonia, showing a thickened contrast-enhanced pleural rind, high-density pleural effusion, loculation, and septation. Thoracentesis yielded foul-smelling pus.

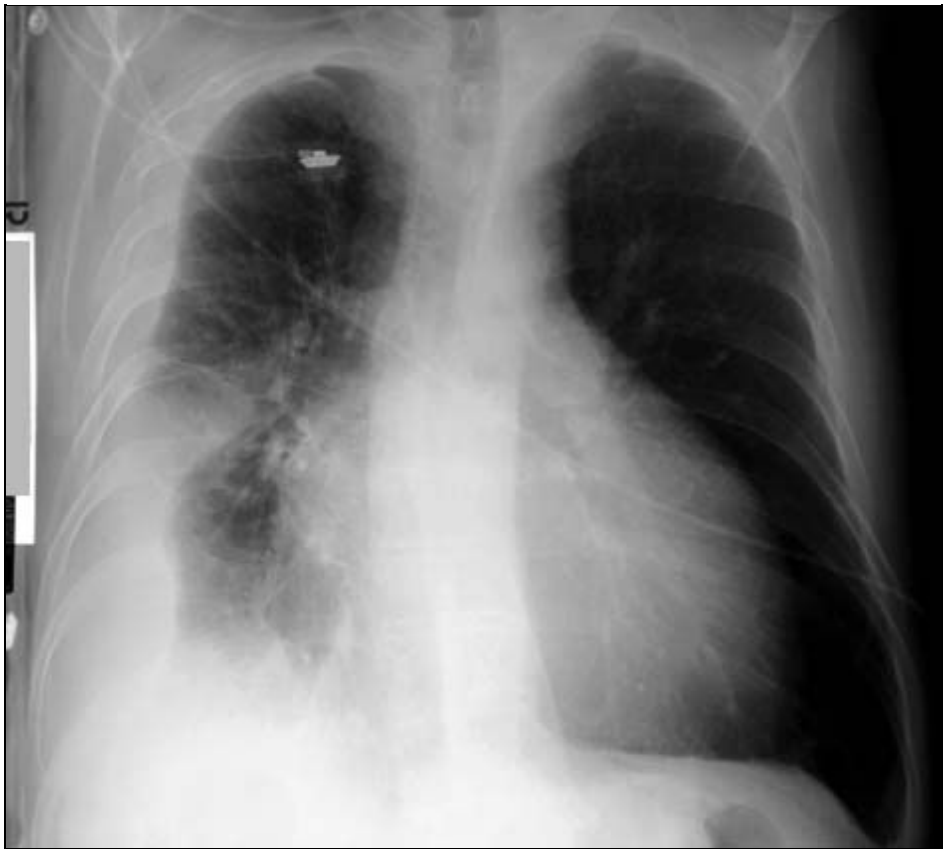
- Pleural enhancement can be seen in patients with active inflammation and severe pleuropulmonary infections, which provides another sign of the possibility of a complicated pleural effusion or empyema.
- CT scanning of the chest may also help detect airway or parenchymal abnormalities such as endobronchial obstruction or the presence of lung abscesses.

Other Tests

While no diagnostic laboratory tests are available for a parapneumonic effusion, serum total protein and lactic dehydrogenase (LDH) levels should be obtained to help characterize whether the pleural fluid is an exudate or transudate. The ratio of pleural fluid/serum protein and LDH is used to distinguish between these two entities.

Procedures

Thoracentesis is recommended when the suspected parapneumonic pleural effusion is greater than or equal to 10 mm thick on a lateral decubitus chest radiograph.[7] See the image below.



A right lateral decubitus chest radiograph shows a free-flowing pleural effusion, which should be sampled with thoracentesis for pH determination, Gram stain, and culture.

Pleural fluid appearance may vary from a clear yellow liquid to an opaque turbid fluid to grossly purulent thick, viscous, foul-smelling pus. Foul-smelling fluid indicates an anaerobic infection.

- Pleural fluid studies
  - Blood cell count (WBC count) and differential: Results generally are not diagnostic, but most transudates are associated with a WBC counts of less than 1000 cells/µL and empyemas are exudates, with WBC counts generally greater than 50,000 cells/µL.
  - Pleural fluid total protein, LDH, and glucose (corresponding serum protein and LDH): Exudates are defined by pleural/serum total protein ratio of greater than 0.5 and a pleural/serum LDH ratio of greater than 0.6 or a pleural fluid LDH value greater than two thirds the upper limit of normal. One criterion is sufficient to classify fluid as an exudate.
  - Pleural fluid pH (iced blood gas syringe): Values of less than 7.20 are suggestive of a complicated pleural effusion.
  - Other laboratories suggestive of complicated pleural effusion or empyema: These include (1) an LDH value of greater than 1000 U/L and a glucose level of less than 40 mg/d of (2) a pH of less than 7.00 and

a glucose level of less than 40 mg/dL.

- Microbiology (Gram stain, bacterial culture): Acid-fast bacilli and fungal infections may cause pleural effusions or empyema, but theses organisms are more difficult to culture from pleural fluid.

Histologic Findings

Multiple granulocytes would be seen on histologic examination, but no specific pattern is recognized. Necrotic debris may be present. Bacteria are seen in the pleural fluid in severe infections.

Staging

The following classification and treatment scheme has been used to characterize parapneumonic effusions and empyema.

- Category 1 (parapneumonic effusion)
  - Minimal free-flowing fluid, smaller than 10 mm on decubitus films
  - Culture, Gram stain, and pH unknown
  - No thoracentesis needed; treatment with antibiotics alone
- Category 2 (uncomplicated parapneumonic effusion)
  - Larger than 10 mm fluid and less than half the hemithorax on decubitus films
  - Gram stain and culture negative
  - pH higher than 7.20
  - Treatment with antibiotics alone
- Category 3 (complicated parapneumonic effusion)
  - Large free-flowing effusion, more than half the hemithorax
  - pH lower than 7.20, LDH level greater than 1000 U/L and glucose level greater than 40 mg/dL
  - Gram stain or culture positive
  - Treatment with tube thoracostomy and antibiotics
  - Multiloculated effusions may require multiple tubes
  - Thrombolytics may help resolution
- Category 4 (empyema)
  - Large free-flowing effusion, greater than equal to half the hemithorax
  - Loculated effusion or effusion with thickened pleura
  - Gross pus on aspiration
  - Treatment with tube thoracostomy
  - Thrombolytics may help resolution
  - May require decortication

Treatment

Medical Care

The initial treatment of a patient with pneumonia and pleural effusion involves 2 major decisions. The first decision involves selection of an appropriate antibiotic that will cover likely pathogens. The second decision involves the need for drainage of pleural fluid and is be guided by the American College of Chest Physicians (ACCP) guideline recommendations for the medical and surgical treatment of parapneumonic effusions.[7]

The initial antibiotic selection is usually based on whether the pneumonia is community or hospital acquired and on the severity of the patient's illness. For a patient with community-acquired pneumonia, the recommended agents are second- or third-generation cephalosporins in addition to a macrolide. For patients hospitalized with severe community-acquired pneumonia, initiate treatment with a macrolide plus a third-generation cephalosporin with antipseudomonal activity. Enteric gram-negative bacilli frequently cause pneumonia acquired in institutions (eg, hospitals, nursing homes). Therefore, initial antibiotic coverage should include an antibiotic effective against pseudomonads. If aspiration is evident or suspected, oral anaerobes should also be covered.

Infectious Diseases Society of America (IDSA)/American Thoracic Society (ATS) consensus guidelines on the management of community-acquired pneumonia, hospital-acquired pneumonia, ventilator-associated pneumonia, and healthcare-associated pneumonia in adults are published elsewhere.[8,9] Also see Pneumonia, Bacterial.

Effusions with pleural fluid layering less than 10 mm on decubitus chest radiographs almost always resolve with appropriate systemic antibiotics. Patients with pleural effusions that have a pleural fluid layering greater than 10 mm on lateral decubitus radiographs must have a diagnostic thoracentesis. If the diagnostic thoracentesis yields thick pus, the patient has an empyema thoracis and definitive pleural drainage is absolutely required. If the pleural fluid is not thick pus, then results of pleural fluid Gram stain or culture, pleural fluid pH and glucose levels, and the presence or absence of pleural fluid loculations should guide the course of action as recommended in the guidelines.[7]

Of note, the strength of recommendations by the expert panel in this guideline is somewhat limited because of the small number of randomized, controlled trials, and methodological weakness resulted in heterogeneous data. The panel urged review of these recommendations cautiously; they purposefully avoided specific recommendations or preferences on primary management approaches (ie, no drainage, therapeutic thoracentesis, tube thoracostomy, fibrinolytics, video-assisted thoracoscopic surgery [VATS], thoracotomy). Despite these limitations, consistent and possibly clinically meaningful trends formed for the pooled data and the results of the randomized, controlled trials and the historically controlled series on the primary management approach to parapneumonic pleural effusions.

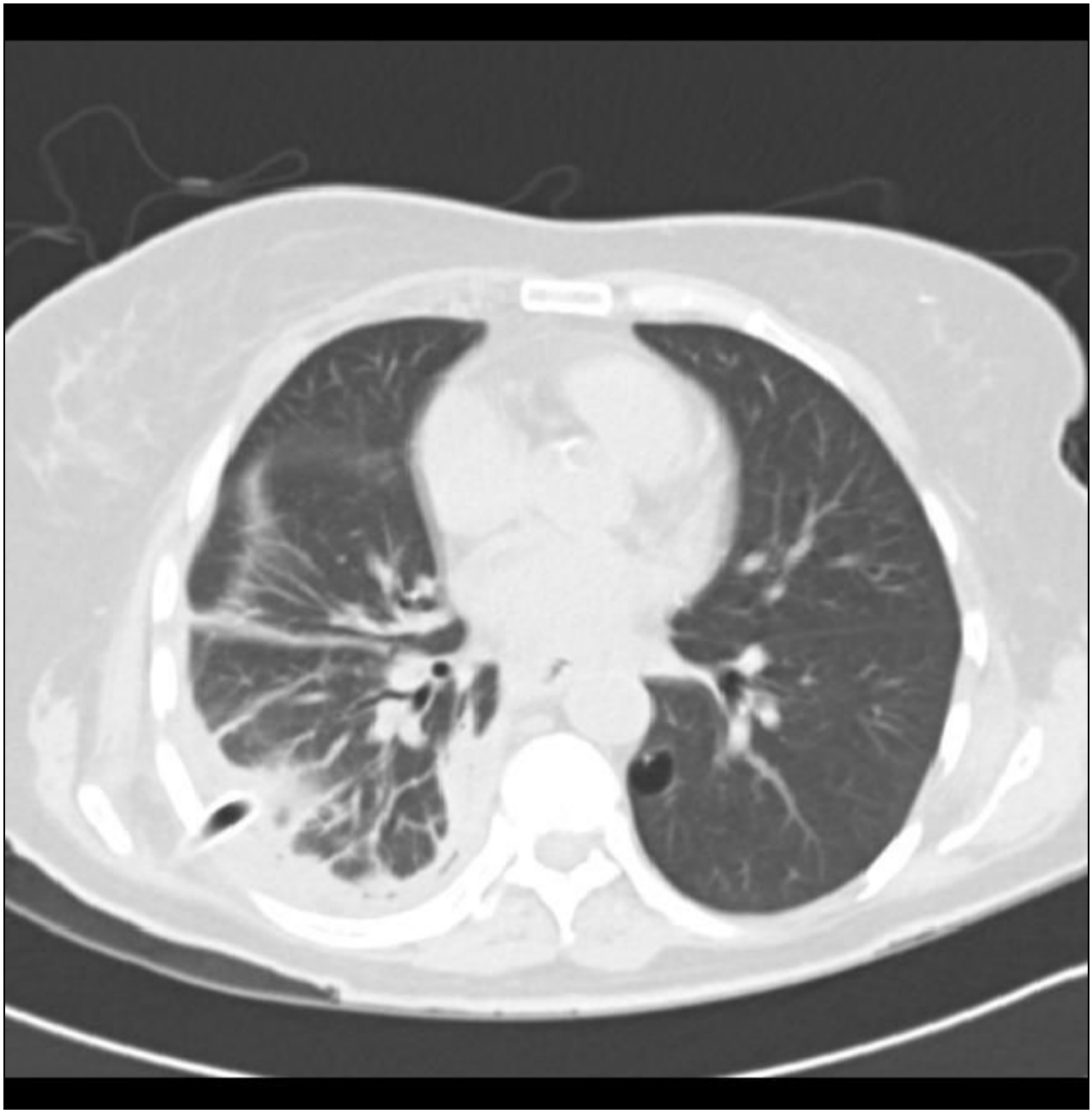
In summary, the recommendations are as follows:

- In all patients with acute bacterial pneumonia, the presence of a parapneumonic pleural effusion should be considered (level C evidence).
- In patients with parapneumonic pleural effusions, the estimated risk for poor outcome, using the panel-recommended approach based on pleural space anatomy, pleural fluid bacteriology, and pleural fluid chemistry, should be the basis for determining whether the parapneumonic pleural effusions should be drained (level D evidence). Poor outcomes could result from 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, and increased mortality. The 4 risk categories are as follows:
  - Category 1 (very low risk): The effusion is small (<10-mm thickness on decubitus) and free flowing (A_0). Because the effusion is small, no thoracentesis is performed and the bacteriology (B_x) and chemistry (C_x) of the fluid are unknown.
  - Category 2 (low risk): The effusion is small to moderate (≥10 mm and less than half the hemithorax) and free flowing (A_1) with negative culture and Gram stain regardless of prior use of antibiotics (B_0); pH is higher than or equal to 7.20 (C_0).
  - Category 3 (moderate risk): The effusion meets one of the following criteria: large (greater than or equal to half the hemithorax), loculated effusion, thicken pleura on contrast-enhanced CT scan (A_2), positive Gram stain or culture (B_1), or pH less than 7.20 (C_1).
  - Category 4 (high risk): This is when pleural fluid consists of pus.

- Patients with category 1 or category 2 risk for poor outcome with parapneumonic pleural effusions may not require drainage (level D evidence).
- Drainage is recommended for management of category 3 or 4 parapneumonic pleural effusions based on pooled data for mortality and the need for second interventions with the no-drainage approach (level C evidence).
- Based on the pooled data for mortality and the need for second interventions, therapeutic thoracentesis or tube thoracostomy alone appears to be insufficient treatment for treating most patients with category 3 or 4 parapneumonic pleural effusions (level C evidence). However, the panel recognizes that in the individual patient, therapeutic thoracentesis or tube thoracostomy, as planned interim steps before a subsequent drainage procedure, may result in complete resolution of the parapneumonic pleural effusions. Careful evaluation of the patient for several hours is essential in these cases. If resolution occurs, no further intervention is necessary (level D evidence).
- Fibrinolytics, VATS, and surgery are acceptable approaches for managing patients with category 3 and category 4 parapneumonic pleural effusions based on cumulative data across all studies that indicate that these interventions are associated with the lowest mortality and need for second interventions (level C evidence).

Chest tubes (tube thoracostomy)

Insert chest tubes immediately after a complicated parapneumonic pleural effusion or empyema thoracis is diagnosed (see the image below). The key to resolution involves prompt drainage of pleural fluid because delay leads to the formation of loculated pleural fluid.



Chest CT scan with intravenous contrast in a patient with mixed Streptococcus milleri and anaerobic empyema following aspiration pneumonia, 3 days following thoracostomy and intrapleural fibrinolysis (Reteplase).

Position the chest tube in a dependent part of the pleural effusion. Previously, large-bore (38-32F) tubes were recommended, but smaller tubes are similarly effective, and at least a 28F tube should be placed. These can be placed either using a guidewire-assisted serial dilatation technique or the more traditional cut-down approach.

Smaller pigtail catheters (8-14F) can also be placed under ultrasound or CT guidance. Consider these in smaller, difficult-to-access, multiple-loculated effusions and nonloculated, nonpurulent effusions. These catheters have also been successful in draining empyemas. The variation in success rates for these catheters (72–82%) is associated with patient selection, operator expertise, and the stage of the parapneumonic pleural effusions. The major advantage of small-bore catheters is better patient tolerance and avoidance of major complications.[1]

Continue closed-tube drainage as long as clinical and radiologic improvement are observed. The chest tube can be removed once the volume of the pleural drainage is less than 100 mL/24 h, with clearance of the pleural fluid turbidity seen in complicated pleural effusions.

If the patient does not demonstrate clinical or radiologic improvement with declining pleural fluid drainage, perform a pleural space ultrasound examination or chest CT scanning to look for pleural fluid loculations and ensure proper tube placement.

Undrained pleural fluid may respond to intrapleural thrombolytic therapy or may require placement of another tube. Closed chest tube drainage yields satisfactory results in approximately 60% of patients with aerobic infections and 25% of patients with anaerobic infections.

Intrapleural thrombolytic agents

Since the 1970s, several studies have reported success of thrombolytic therapy for loculated complicated parapneumonic pleural effusions.[10,11,12,13,14,15,16,17,18] The thrombolytic agents used in parapneumonic pleural effusions are more effective if administered in the early fibrinopurulent stage of parapneumonic pleural effusions.

With thrombolytic therapy, success rates of 70-90% have been reported. Streptokinase has been used in a dose of 250,000 IU in 100 mL of normal saline once or twice a day. Urokinase was also effective and in a randomized trial of patients with multiloculated pleural effusions. Subjects in the urokinase group drained significantly more pleural fluid, required less surgical intervention, and required fewer days in the hospital.

Following instillation, the chest tube is clamped for 2-4 hours. These agents may be administered daily for as many as 14 days. Streptokinase may lead to sensitization with production of an antibody response and subsequent allergic reaction if used for systemic thrombolysis.

Streptokinase and urokinase are probably equally effective, although neither has been compared to each other in a research trial. The potential for developing antibodies to streptokinase has generally favored urokinase as a pleural thrombolytic. However, urokinase is not currently commercially available.

While thrombolytic agents may facilitate and increase pleural fluid drainage, their effect on improving patient outcomes and avoiding surgical intervention has not been established.

A prospective randomized trial of intrapleural thrombolytic agent streptokinase (MIST1 group) was conducted on the drainage of infected pleural fluid collections. In this double-blind trial, 454 patients with pleural infection (either purulent pleural fluid or pleural fluid with a pH <7.20 with signs of infection) received either intrapleural streptokinase (250,000 IU bid for 3 d) or placebo. Among the 427 patients who received streptokinase or placebo, no benefit was reported for streptokinase in terms of mortality, rate of surgery, radiographic outcomes, or length of hospital stay; serious adverse events (chest pain, fever, or allergy) were more common with streptokinase.[14]

Tokuda et al performed a meta-analysis of all properly randomized trials, comparing intrapleural thrombolytic agents with placebo in adult patients with empyema thoracis and complicated parapneumonic pleural effusions. The outcome of primary interest was the reduction of death and surgical intervention. Five trials totaling 575 patients were included.[15]

The MIST1 trial constituted the bulk of patients in the meta-analysis, and its nonbeneficial findings contributed significantly to the final conclusion. The meta-analysis did not support the routine use of thrombolytic therapy for all patients who required chest tube drainage for empyema thoracis or complicated parapneumonic pleural effusions.

Note that the meta-analysis described a nonsignificant reduction in death and surgery even despite including the MIST1 trial. Because of significant heterogeneity of the treatment effects, selected patients might benefit from thrombolytic treatment.[15]

Intrapleural recombinant tissue plasminogen activator (r-TPA) or alteplase has been successfully evaluated in pediatric patients with complicated parapneumonic pleural effusion and pleural empyema. Some authors have suggested that r-TPA might be a more effective therapeutic agent than streptokinase.

A small, noncomparative study of consecutive adult patients using r-TPA or alteplase administered intrapleurally in a single daily dose of 25 mg reported the treatment was well tolerated and effective.[16] Another retrospective review of

22 consecutive patients also demonstrated improved drainage of pleural fluid with alteplase, with 2 mg administered into the pleural space 3 times a day for 3 days.

This has led to a prospective, randomized comparison of alteplase with placebo in the management of complicated pleural effusions and empyema. The study has been completed, and the final report of this experience is pending.

The latest Cochrane Database systematic review on this topic published in 2008 had identified 7 studies and 761 patients.[18] A significant reduction in the need for surgical intervention was identified, but the authors also noted the discrepancy between this conclusion and results of the MIST1 trial. The authors note subgroup analysis that suggests the greatest benefit is in patients with loculated effusions, but the data are very limited and due caution is advised. No increase in adverse events was noted with thrombolytic therapy.

Surgical Care

Thoracoscopy

Thoracoscopy is an alternate therapy for multiloculated empyema thoracis. In patients with multiloculated parapneumonic pleural effusions, the loculations in the pleural space can be disrupted with a thoracoscope, and the pleural space can be drained completely. If extensive adhesions are present or thick pleural peel entraps the lung, the procedure may be converted to open thoracostomy and decortication.

Luh et al published their experience in the treatment of complicated parapneumonic pleural effusions and empyema thoracis by VATS in 234 patients (108 women, 126 men). More than 85% (200 patients) received preoperative diagnostic or therapeutic thoracentesis, tube thoracostomy, or fibrinolytics. Of 234 patients, 202 patients (86.3%) achieved satisfactory results with VATS. Only 40 patients required open decortication or repeat procedures. VATS is safe and effective for treatment; earlier intervention with VATS can produce better clinical results.[19]

Hope et al reviewed outcomes of surgical treatment for parapneumonic empyema thoracis. The use of VATS was compared with thoracotomy. Morbidity and mortality rates were similar among all groups. The conversion rate to open thoracotomy was 21%. Based on a shorter postoperative length of stay with similar morbidity and mortality in patients operated on within 11 days of admission, early aggressive surgery treatment for complicated parapneumonic effusions or empyema thoracis is recommended.[20]

Retrospective evaluation of 2 different surgical procedures (decortication vs debridement) and approaches (VATS vs thoracotomy) were analyzed by Casali and colleagues. The study included 119 patients; 51 patients had debridement (52% through VATS, 48% through thoracotomy) and 68 patients had decortications through thoracotomy. VATS debridement had a lower postoperative hospital stay and shorter duration of chest drainage and greater improvement in a subjective dyspnea score. The long-term spirometric evaluation was normal in 58 patients (56%). Age older than 70 years old was the only variable associated with poor long-term results (forced expiratory volume in 1 second [FEV_1] <60% and/or dyspnea Medical Research Council grade ≥2) at multivariate analysis. VATS is associated with less postoperative mortality and shorter postoperative hospital stay.[21]

Two other studies that support the use of VATS as a primary drainage procedure are those by Potaris et al[22] and Chan et al.[23]

Wang and colleagues proposed a new technique using an electronic endoscope (bronchoscope or gastroscope) inserted through the chest tube to directly visualize, irrigate, and break down the loculation effectively in various pleural diseases, including 13 cases of empyema thoracis.[24]

In a prospective, randomized study comparing VATS and thrombolytic therapy in children with empyema, no differences in outcomes were noted between the 2 methods in a small study involving 36 patients.[25] Thrombolytic therapy consisted of 4-mg doses administered 3 times over a 48-hour period. Three (16.7%) of the patients treated with thrombolytic therapy eventually required VATS for management.

Rib resection and open drainage of pleural space

Open drainage of the pleural space may be used when closed-tube drainage of the pleural infection is inadequate and

the patient does not respond to intrapleural thrombolytic agents. This procedure is recommended only when the patient is too ill to tolerate decortication. The resection of 1-3 ribs overlying the lower part of the empyema thoracis cavity is performed, a large-bore chest tube is inserted into the empyema thoracis cavity, and the tube is drained into a colostomy bag.

Patients treated by open drainage have an open chest wound for a prolonged period. In one series, the median time for healing the drainage site was 142 days. With decortication, the period of convalescence is much shorter, although patients who are markedly debilitated do not tolerate decortication.

In decortication, all the fibrous tissue is removed from the visceral pleural peel, and all pus is evacuated from the pleural space. Decortication is a major thoracic operation requiring full thoracotomy; therefore, decortication is not tolerated by critically ill patients. Decortication is the procedure of choice for patients in whom pleural sepsis is not controlled by closed-tube thoracostomy, intrapleural thrombolytic agents, and, possibly, thoracoscopy. Mortality rates as high as 10% have been described with this procedure. Decortication should not be performed solely to remove the thickened pleural peel; the thickened pleural peel usually resolves over several months. If the pleura remains thickened with symptom-limiting reduction in pulmonary function after approximately 6 months, decortication can be considered.

Postpneumonectomy empyema thoracis, an uncommon but life-threatening complication, is often associated with a bronchopleural fistula. Treatment of bronchopleural fistula depends on several factors, including the extent of dehiscence, degree of pleural contamination, and general condition of the patient. Early diagnosis and aggressive therapeutic strategies for controlling infection, closing the fistula, and sterilizing the closed pleural space are mandatory. Repeated debridement, VATS, endoscopic application of tissue glue, and stenting may be additional management strategies.[26]

Consultations

- Most patients can be treated by pulmonary and/or infectious diseases specialists.
- An interventional radiologist may be needed to place small-bore drainage catheters for difficult-to-access loculated effusions.
- Patients with persistently loculated effusions or unresolving empyema thoracis may require surgery and should be seen by a thoracic surgeon.

Diet

No dietary restrictions are recommended for patients with parapneumonia effusions and empyema, other than what is dictated by comorbidities.

Activity

No specific activity restrictions are recommended for patients with parapneumonic effusions and empyema. Their activity level may be limited by comorbidities and any interventions required to treat their infection.

Medication

The goals of pharmacotherapy are to reduce morbidity and prevent complications.

Antibiotics

Therapy must be comprehensive and cover all likely pathogens in the context of this clinical setting. Initiate therapy with intravenous antibiotics and transition to oral agents or equivalent agents based on clinical response. Oral antibiotics can be used to transition from intravenous therapy; they allow completion of a full course of therapy without the need for intravascular access or inpatient hospitalization.

The antibiotic choice should focus on the most likely pathogens, ranging from anaerobic infections to community-acquired pathogens, to nosocomial or healthcare–associated pathogens, to resistant Gram-positive pneumonias.

Penicillin G (Pfizerpen)

Interferes with synthesis of cell wall mucopeptide during active multiplication, resulting in bactericidal activity against susceptible microorganisms.

Dosing

Adult

2 million U IV q4h

Pediatric

150,000 U/kg/d IV q4h

Interactions

Probenecid can increase effects; coadministration of tetracyclines can decrease effects

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Caution in impaired renal function

Penicillin VK (Beepen-VK, Betapen-VK, Pen.Vee K, Robicillin VK, V-Cillin K, Veetids)

Preferred to penicillin G because of increased resistance to gastric acid. Treatment must continue for 10 full days. The probability of relapse of a GAS infection after therapy is 50% if penicillin is discontinued after 3 d of therapy.

Dosing

Adult

500 mg PO q6-8h for 10 d

Pediatric

25-50 mg/kg/d PO divided tid/qid; not to exceed 3 g/d

Interactions

Probenecid may increase effectiveness by decreasing clearance; tetracyclines are bacteriostatic, causing a decrease in effectiveness of penicillins when administered concurrently

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Caution in renal impairment

Amoxicillin (Amoxil, Biomox, Trimox)

Has better absorption than penicillin VK and administration is q8h instead of q6h. For minor infections, some authorities advocate administration q12h. Probably most active of penicillins for non–penicillin-susceptible *S pneumoniae*.

Dosing

Adult

0.5-1 g PO q8h

Pediatric

6.7-13.3 mg/kg PO q8h

Interactions

Reduces the efficacy of oral contraceptives

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Adjust dose in renal impairment; may enhance chance of candidiasis

Ampicillin and sulbactam (Unasyn)

Drug combination of beta-lactamase inhibitor with ampicillin. Interferes with bacterial cell wall synthesis during active replication, causing bactericidal activity against susceptible organisms. Alternative to amoxicillin when unable to take medication orally.
Covers skin, enteric flora, and anaerobes. Not ideal for nosocomial pathogens.

Dosing

Adult

1.5 (1 g ampicillin plus 0.5 g sulbactam) to 3 g (2 g ampicillin plus 1 g sulbactam) IV/IM q 6-8h; not to exceed 4 g/d sulbactam or 8 g/d ampicillin

Pediatric

<3 months: Not established
3 months to 12 years: 100-200 mg ampicillin/kg/d (150-300 mg Unasyn) IV divided q6h
>12-years: Administer as in adults; not to exceed 4 g/d sulbactam or 8 g/d ampicillin

Interactions

Probenecid and disulfiram elevate ampicillin levels; allopurinol decreases effects and has additive effects on ampicillin rash; may decrease effects of oral contraceptives

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Adjust dose in renal failure; evaluate rash and differentiate from hypersensitivity reaction

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Clindamycin (Cleocin)

Semisynthetic antibiotic produced by 7(S)-chloro-substitution of 7(R)-hydroxyl group of parent compound lincomycin. Inhibits bacterial growth, possibly by blocking dissociation of peptidyl tRNA from ribosomes, causing RNA-dependent protein synthesis to arrest. Widely distributes in the body without penetration of CNS. Protein bound and excreted by the liver and kidneys.
Available in parenteral form (ie, clindamycin phosphate) and oral form (ie, clindamycin hydrochloride). Oral clindamycin absorbed rapidly and almost completely and is not appreciably altered by presence of food in stomach. Appropriate serum levels reached and sustained for at least 6 h following oral dose. No significant levels are attained in cerebrospinal fluid. Also effective against aerobic and anaerobic streptococci (except enterococci).

Dosing

Adult

600 mg IV q8h; continue treatment with 300 mg PO q6h; doses as high as 4800 mg qd have been used in severe life-threatening infections

Pediatric

8-20 mg/kg/d PO as hydrochloride and 8-25 mg/kg/d IV as palmitate divided tid/qid
Alternatively, 20-40 mg/kg/d IV/IM equally divided tid/qid
Use higher dose for more severe infections

Interactions

Increases duration of neuromuscular blockade induced by tubocurarine and pancuronium; erythromycin may antagonize effects of clindamycin; antidiarrheals may delay absorption

Contraindications

Documented hypersensitivity; regional enteritis, ulcerative colitis, hepatic impairment, antibiotic-associated colitis

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Adjust dose in severe hepatic dysfunction; no adjustment necessary in renal insufficiency; associated with severe and possibly fatal colitis by allowing overgrowth of *Clostridium difficile*

Moxifloxacin (Avelox)

Inhibits the A subunits of DNA gyrase, resulting in inhibition of bacterial DNA replication and transcription. Indicated for community-acquired pneumonia, including multidrug-resistant *S pneumoniae*.

Dosing

Adult

400 mg PO/IV qd

Pediatric

<18 years: Not recommended
>18 years: Administer as in adults

Interactions

Antacids and electrolyte supplements reduce absorption; loop diuretics, probenecid, and cimetidine increase serum levels; NSAIDs enhance CNS stimulating effect
May increase toxicity of theophylline, caffeine, cyclosporine, and digoxin (monitor digoxin levels); may increase effects of anticoagulants (monitor PT); ferrous sulfate decreases bioavailability (administer moxifloxacin 4 h prior or 8 h following ferrous sulfate); coadministration with drugs that prolong QTc interval (quinidine, procainamide, amiodarone, sotalol, erythromycin, TCAs) increase risk of life-threatening arrhythmia

Contraindications

Documented hypersensitivity; known Q-T prolongation, concurrent administration of drugs that cause Q-T prolongation

Precautions

Pregnancy

X - Contraindicated; benefit does not outweigh risk

Precautions

In prolonged therapy, perform periodic evaluations of organ system functions (eg, renal, hepatic, hematopoietic); superinfections may occur with prolonged or repeated antibiotic therapy; fluoroquinolones have induced seizures in CNS disorders and caused tendinitis or tendon rupture

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Amoxicillin and clavulanate (Augmentin, Augmentin XR)

Inhibits bacterial cell wall synthesis by binding to penicillin-binding proteins. Addition of clavulanate inhibits beta-lactamase producing bacteria.
Good alternative antibiotic for patients allergic to or intolerant of macrolide class. Usually well tolerated and provides good coverage of most infectious agents. Not effective against *Mycoplasma* and *Legionella* species. Half-life of oral dosage form is 1-1.3 h. Has good tissue penetration but does not enter cerebrospinal fluid.
For children >3 mo, base dosing on amoxicillin content. Due to different amoxicillin/clavulanic acid ratios in 250-mg tab (250/125) vs 250-mg chewable tab (250/62.5), do not use 250-mg tab until child weighs >40 kg.

Dosing

Adult

500 - 875 mg q12h PO or 500 mg PO q8h for 7-10 d

Pediatric

<3 months: 125 mg/5 mL PO susp based on amoxicillin; 30 mg/kg/d divided bid for 7-10 d
>3 months: if using 200 mg/5 mL or 400 mg/5 mL susp, 45 mg/kg/d PO q12h; if using 125 mg/5 mL or 250 mg/5 mL susp, 40 mg/kg/d PO q8h for 7-10 d
>40 kg: Administer as in adults

Interactions

Coadministration with warfarin or heparin increases risk of bleeding; may act synergistically against selected microorganisms when coadministered with aminoglycosides; coadministration with allopurinol may increase incidence of amoxicillin rash; may decrease efficacy of oral contraceptives when administered concomitantly

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Hepatic impairment may occur with prolonged treatment in elderly persons; diarrhea may occur; adjust dose in renal impairment; cross-allergy may occur with other beta-lactams and cephalosporins

Cefoxitin (Mefoxin)

Second-generation cephalosporin with activity against some gram-positive cocci, gram-negative rod infections, and anaerobic bacteria. Inhibits bacterial cell wall synthesis by binding to one or more of the penicillin-binding proteins; inhibits final transpeptidation step of peptidoglycan synthesis, resulting in cell wall death.
Infections caused by cephalosporin- or penicillin-resistant gram-negative bacteria may respond to cefoxitin.

Dosing

Adult

1-2 g IV/IM q6-8h or 1-2 g IV/IM q4h in severe cases

Pediatric

80-160 mg/kg/d IV in 4-6 divided doses

Interactions

Probenecid may increase effects of cefoxitin; coadministration with aminoglycosides or furosemide may increase nephrotoxicity (closely monitor renal function)

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Adjust dose in severe renal insufficiency (high doses may cause CNS toxicity); superinfections and promotion of nonsusceptible organisms may occur with prolonged use or repeated therapy

Ceftriaxone (Rocephin)

Third-generation cephalosporin with broad-spectrum, gram-negative activity; lower efficacy against gram-positive organisms; higher efficacy against resistant organisms. Bactericidal activity results from inhibiting cell wall synthesis by binding to one or more penicillin-binding proteins. Exerts antimicrobial effect by interfering with synthesis of peptidoglycan, a major structural component of bacterial cell wall. Bacteria eventually lyse because of the ongoing activity of cell wall autolytic enzymes while cell wall assembly is arrested.
Highly stable in presence of beta-lactamases, both penicillinase and cephalosporinase, of gram-negative and gram-positive bacteria. Approximately 33-67% of dose excreted unchanged in urine, and remainder secreted in bile and

ultimately in feces as microbiologically inactive compounds. Reversibly binds to human plasma proteins, and binding has been reported to decrease from 95% bound at plasma concentrations <25 mcg/mL to 85% bound at 300 mcg/mL.

Dosing

Adult

500-1000 mg IV q12h; not to exceed 4 g/d

Pediatric

Neonates >7 d: 25-50 mg/kg/d IV/IM; not to exceed 125 mg/d
Infants and children: 50-75 mg/kg/d IV/IM divided q12h; not to exceed 2 g/d

Interactions

Probenecid may increase ceftriaxone levels; coadministration with ethacrynic acid, furosemide, and aminoglycosides may increase nephrotoxicity; simultaneous administration with IV calcium-containing solutions may cause precipitation (thoroughly flush infusion lines between ceftriaxone and calcium)

Contraindications

Documented hypersensitivity; hyperbilirubinemic neonates, particularly those who are premature; neonates ≤28 d if they receive calcium-containing IV products

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Adjust dose in severe renal insufficiency (high doses may cause CNS toxicity); superinfections and promotion of nonsusceptible organisms may occur with prolonged use or repeated therapy; caution in breastfeeding; may displace bilirubin from albumin-binding sites, increasing risk of kernicterus; caution with gallbladder, biliary tract, liver, or pancreatic disease; caution in patients with history of colitis or penicillin hypersensitivity

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Cefepime (Maxipime)

Fourth-generation cephalosporin. Gram-negative coverage comparable to ceftazidime but has better gram-positive coverage (comparable to ceftriaxone). Cefepime is a zwitter ion; rapidly penetrates gram-negative cells. Best beta-lactam for IM administration. Poor capacity to cross blood-brain barrier precludes use for treatment of meningitis. May be more active than ceftazidime against *Enterobacter* species because of enhanced stability against beta-lactamases.
May be more active than ceftazidime against Enterobacter species because of its enhanced stability against beta lactamases.

Dosing

Adult

2 g IV q12h

Pediatric

50 mg/kg IV q8h

Interactions

Probenecid may increase effects of cefepime; aminoglycosides increase nephrotoxic potential of cefepime

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Dosage adjustments (adult adjustments)
CrCl (mL/min) 80-50: 0.5-2 g q12-24h
CrCl 50-10: 0.5-2 g/d
CrCl <10: 0.25-0.5 g/d
Hemodialysis: Same as for CrCl <10, with an extra 0.25 g after hemodialysis
During peritoneal dialysis: 1-2 g q48h
High doses may cause CNS toxicity; prolonged use may predispose patients to superinfection

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Cefuroxime (Ceftin, Kefurox, Zinacef)

Second-generation cephalosporin maintains gram-positive activity of first-generation cephalosporins; adds activity against *Proteus mirabilis, Haemophilus influenzae, Escherichia coli, Klebsiella pneumoniae,* and *Moraxella catarrhalis*.
Binds to penicillin-binding proteins and inhibits final transpeptidation step of peptidoglycan synthesis, resulting in cell wall death. Condition of patient, severity of infection, and susceptibility of microorganism determine proper dose and route of administration. Resists degradation by beta-lactamase.

Dosing

Adult

750 mg to 1.5 g IV q8h for 10 d
250-500 mg PO bid for 10 d

Pediatric

Neonates: 20-50 mg/kg/d IV divided q12h
Infants and children: 75-150 mg/kg/d IV divided q8h; not to exceed 6 g/d
<13 years: 250 mg PO bid for 20 d
>13 years: Administer as in adults

Interactions

Disulfiramlike reactions may occur when alcohol is consumed within 72 h after taking cefuroxime; may increase hypoprothrombinemic effects of anticoagulants; may increase nephrotoxicity in patient receiving potent diuretics such as loop diuretics; coadministration with aminoglycosides increases nephrotoxic potential

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Reduce dosage by half if CrCl is 10-30 mL/min and by three quarters if <10 mL/min (high doses may cause CNS toxicity); bacterial or fungal overgrowth of nonsusceptible organisms may occur with prolonged or repeated therapy

Cefaclor (Ceclor)

Second-generation cephalosporin that binds to one or more of the penicillin-binding proteins, which, in turn, inhibits cell wall synthesis and results in bactericidal activity. Has gram-positive activity that first-generation cephalosporins have and adds activity against *P mirabilis, H influenzae, E coli, K pneumoniae,* and *M catarrhalis*. Indicated for infections caused by susceptible mixed aerobic-anaerobic microorganisms. Determine proper dosage and route based on condition of patient, severity of infection, and susceptibility of causative organism.

Dosing

Adult

750-1500 mg/d PO divided bid/tid for 10-14 d

Pediatric

<1 month: Administer as in adults
>1 month: 20-40 mg/kg/d PO divided q8-12h; not to exceed 2 g/d for 10-14 d

Interactions

Alcoholic beverages consumed <72 h after taking cefaclor may produce disulfiramlike reactions; may increase hypoprothrombinemic effects of anticoagulants; coadministration with potent diuretics and aminoglycosides (eg, loop diuretics) may increase nephrotoxicity

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Reduce dosage by half if CrCl 10-30 mL/min and by three quarters <10 mL/min (high doses may cause CNS toxicity); bacterial or fungal overgrowth of nonsusceptible organisms may occur with prolonged or repeated therapy

Piperacillin and tazobactam sodium (Zosyn)

Nosocomial pneumonia caused by *P aeruginosa* should be treated in combination with an aminoglycoside. Antipseudomonal penicillin plus beta-lactamase inhibitor. Inhibits biosynthesis of cell wall mucopeptide and is effective during stage of active multiplication.

Dosing

Adult

4.5 g IV q6h

Pediatric

<12 years: Not established
>12 years: Administer as in adults

Interactions

Tetracyclines may decrease effects of piperacillin; high concentrations of piperacillin may physically inactivate aminoglycosides if administered in same IV line; effects when administered concurrently with aminoglycosides are

synergistic; probenecid may increase penicillin levels; high dose parenteral penicillins may result in increased risk of bleeding

Contraindications

Documented hypersensitivity; severe pneumonia, bacteremia, pericarditis, emphysema, meningitis, and purulent or septic arthritis should not be treated with an oral penicillin during acute stage

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Perform CBC counts prior to initiation of therapy and at least qwk during therapy; monitor for liver function abnormalities by measuring AST and ALT during therapy; exercise caution in patients diagnosed with hepatic insufficiencies; perform urinalysis and BUN and creatinine determinations during therapy and adjust dose if values become elevated; monitor blood levels to avoid possible neurotoxic reactions

Cefprozil (Cefzil)

Second-generation cephalosporin that binds to one or more of the penicillin-binding proteins, which, in turn, inhibits cell wall synthesis and results in bactericidal activity. Has gram-positive activity that first-generation cephalosporins have and adds activity against *P mirabilis, H influenzae, E coli, K pneumoniae,* and *M catarrhalis*. Condition of patient, severity of infection, and susceptibility of microorganism determine proper dose and route of administration.

Dosing

Adult

500 mg/d PO for 10 d

Pediatric

<12 years: 30 mg/kg/d PO divided q12h for 10 d
>12 years: Administer as in adults

Interactions

Probenecid increases effect; coadministration with furosemide and aminoglycosides increases nephrotoxic effects

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Adjust dose in severe renal insufficiency (high doses may cause CNS toxicity); superinfections and promotion of nonsusceptible organisms may occur with prolonged use or repeated therapy; caution with history of GI disease, especially colitis

Levofloxacin (Levaquin)

Rapidly becoming a popular choice in pneumonia. Good monotherapy for pseudomonal infections and infections due

to multidrug-resistant gram-negative organisms.

Dosing

Adult

500-750 mg/d PO/IV for 7-14 d

Pediatric

<18 years: Not recommended
>18 years: Administer as in adults

Interactions

Antacids, iron salts, and zinc salts may reduce serum levels; administer antacids 2-4 h before or after taking fluoroquinolones; cimetidine may interfere with metabolism of fluoroquinolones; levofloxacin reduces therapeutic effects of phenytoin; probenecid may increase levofloxacin serum concentrations

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

X - Contraindicated; benefit does not outweigh risk

Precautions

In prolonged therapy, perform periodic evaluations of organ system functions (eg, renal, hepatic, hematopoietic); adjust dose in renal function impairment; superinfections may occur with prolonged or repeated antibiotic therapy

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Ertapenem (Invanz)

Bactericidal activity results from inhibition of cell wall synthesis and is mediated through ertapenem binding to penicillin-binding proteins. Stable against hydrolysis by a variety of beta-lactamases including penicillinases, cephalosporinases, and extended-spectrum beta-lactamases. Hydrolyzed by metallo-beta-lactamases. Indicated for community-acquired pneumonia due to S pneumoniae (penicillin-susceptible isolates only), including cases with concurrent bacteremia, *H influenzae* (beta-lactamase–negative isolates only, or *M catarrhalis*).

Dosing

Adult

1 g IV qd
CrCl $\leq$30 mL/min/1.73 m^2: 500 mg IV qd

Pediatric

<3 months: Not established
3 months to 12 years: 15 mg/kg IV q12h; not to exceed 1 g/d
>12 years: Administer as in adults

Interactions

Probenecid may reduce renal clearance of ertapenem and increase half-life but benefit is minimum and does not justify coadministration

Contraindications

Documented hypersensitivity to drug or amide type anesthetics

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Pseudomembranous colitis may occur; seizures and CNS adverse reactions may occur; when using with lidocaine to administer intramuscularly, avoid inadvertent injection into blood vessel; decrease dose in renal failure; serious and occasionally fatal hypersensitivity reactions may occur with beta-lactams, caution with previous hypersensitivity reactions to penicillin, cephalosporins, other beta-lactams, or other allergens; do not mix or co-infuse in same IV line as other medications; do not mix with dextrose-containing diluents

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Clarithromycin (Biaxin)

Semisynthetic macrolide antibiotic that reversibly binds to P site of 50S ribosomal subunit of susceptible organisms and may inhibit RNA-dependent protein synthesis by stimulating dissociation of peptidyl t-RNA from ribosomes, causing bacterial growth inhibition.

Dosing

Adult

500 mg PO bid for 10 d

Pediatric

<6 months: Not recommended
>6 months: 7.5 mg/kg PO bid for 10 d; not to exceed 1 g/d

Interactions

Toxicity increases with coadministration of fluconazole and pimozide; effects decrease and adverse GI effects may increase with coadministration of rifabutin or rifampin; may increase toxicity of anticoagulants, cyclosporine, tacrolimus, digoxin, carbamazepine, ergot alkaloids, triazolam, and HMG-CoA reductase inhibitors
Plasma levels of certain benzodiazepines may increase, prolonging CNS depression; arrhythmias and increases in QTc intervals occur with disopyramide; coadministration with omeprazole may increase plasma levels of both agents; decreases metabolism of repaglinide, thus increasing serum levels and effects

Contraindications

Documented hypersensitivity; coadministration of pimozide

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Coadministration with ranitidine or bismuth citrate not recommended with CrCl <25 mL/min; give half dose or increase dosing interval if CrCl <30 mL/min; diarrhea may be sign of pseudomembranous colitis; superinfections may occur with prolonged or repeated antibiotic therapies

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Imipenem and cilastatin (Primaxin)

Extremely potent broad-spectrum beta-lactam antibiotic. Rapidly hydrolyzed by enzyme dehydropeptidase I located on brush border of renal tubular cells, hence its combination with cilastatin (a reversible inhibitor of dehydropeptidase

I). For treatment of multiple-organism infections in which other agents do not have wide-spectrum coverage or are contraindicated because of potential for toxicity.

Dosing

Adult

Base initial dose on severity of infection and administer in equally divided doses
500 mg IV q6h; not to exceed 3-4 g/d
500-750 mg IM or intra-abdominally q12h

Pediatric

Infants >3 months and children <12 years: 15-25 mg/kg/dose IV q6h
Fully susceptible organisms: Not to exceed 2 g/d
Moderately susceptible organisms: Not to exceed 4 g/d
>12 years: Administer as in adults

Interactions

Coadministration with cyclosporine may increase adverse CNS effects of both agents; coadministration with ganciclovir may result in generalized seizures

Contraindications

Documented hypersensitivity; known hypersensitivity to amide local anesthetics; children with CNS infections (increased seizure risk); children <30 kg with renal impairment (lack of data)

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Adjust dose in renal insufficiency (adult adjustments)
CrCl (mL/min) 80-50: 0.5 g q6-8h
CrCl 50-10: 0.5 g q8-12h
Hemodialysis: 0.25-0.5 g after hemodialysis, then q12h
Adjust dose in renal insufficiency; avoid use in children <12 y with CNS infections
Caution with history of seizures, hypersensitivity to penicillins, cephalosporins, or other beta-lactam antibiotics

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Meropenem (Merrem IV)

A carbapenem, not a beta-lactam antibiotic. Bactericidal broad-spectrum carbapenem antibiotic that inhibits cell wall synthesis. Effective against most gram-positive and gram-negative bacteria. Has slightly increased activity against gram-negative bacteria and a slightly decreased activity against staphylococci and streptococci compared with imipenem.

Dosing

Adult

1 g IV q8h (normal renal function)

Pediatric

<10 years: Not established
>10 years: Administer as in adults

Interactions

Probenecid may inhibit renal excretion, increasing meropenem levels

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Dosage adjustments (adult adjustments)
CrCl (mL/min) 10-50: 0.5-1 g q12h
CrCl <10: 0.5 g/d
Hemodialysis: As for CrCl <10, with an extra 0.5 g after hemodialysis
Pseudomembranous colitis and thrombocytopenia may occur, requiring immediate discontinuation

Azithromycin (Zithromax)

Acts by binding to 50S ribosomal subunit of susceptible microorganisms and blocks dissociation of peptidyl tRNA from ribosomes, causing RNA-dependent protein synthesis to arrest. Nucleic acid synthesis not affected.
Concentrates in phagocytes and fibroblasts as demonstrated by in vitro incubation techniques. In vivo studies suggest concentration in phagocytes may contribute to drug distribution to inflamed tissues.
Treats mild-to-moderate microbial infections.
Plasma concentrations are very low, but tissue concentrations are much higher, giving it value in treating intracellular organisms. Has a long tissue half-life.
Newer macrolides offer decreased GI upset and potential for improved compliance through reduced dosing frequency.
Also afford more improved action against *H influenzae* compared with erythromycin.

Dosing

Adult

Day 1: 500 mg PO
Days 2-5: 250 mg PO qd
500 mg IV q24h for 3 d, then 500 mg/d PO for 7-10 d

Pediatric

<6 months: Not established
>6 months:
Day 1: 10 mg/kg PO once; not to exceed 500 mg/d
Days 2-5: 5 mg/kg PO qd; not to exceed 250 mg/d

Interactions

May increase toxicity of theophylline, warfarin, and digoxin; effects are reduced with coadministration of aluminum and/or magnesium antacids; nephrotoxicity and neurotoxicity may occur when coadministered with cyclosporine

Contraindications

Documented hypersensitivity; hepatic impairment; do not administer with pimozide

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Site reactions can occur with IV route; bacterial or fungal overgrowth may result from prolonged antibiotic use; may increase hepatic enzyme levels and cholestatic jaundice; caution in patients with impaired hepatic function or prolonged QT intervals

Vancomycin (Lyphocin, Vancocin, Vancoled)

Classified as glycopeptide agent that has excellent gram-positive coverage, including methicillin-resistant *S aureus*. To avoid toxicity, current recommendation is to assay vancomycin trough levels after third dose drawn 0.5 h prior to next dosing. Use CrCl to adjust dose in patients diagnosed with renal impairment.

Dosing

Adult

500 mg IV q6h or 1 g IV q12h; not to exceed 10 mg/min

Pediatric

40 mg/kg/d IV divided tid/qid

Interactions

Erythema, histaminelike flushing, and anaphylactic reactions may occur when administered with anesthetic agents; taken concurrently with aminoglycosides, risk of nephrotoxicity may increase above that with aminoglycoside monotherapy; effects in neuromuscular blockade may be enhanced when coadministered with nondepolarizing muscle relaxants

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Caution in renal failure and neutropenia; red man syndrome is caused by IV infusion that is too rapid (dose given over a few minutes) but rarely happens when dose given IV over 2 h administration or as PO or IP administration; red man syndrome is not an allergic reaction

Linezolid (Zyvox)

Prevents formation of functional 70S initiation complex, which is essential for bacterial translation process. Bacteriostatic against enterococci and staphylococci and bactericidal against most strains of streptococci. Used as alternative in patients allergic to vancomycin and for treatment of vancomycin-resistant enterococci.

Dosing

Adult

600 mg PO/IV q12h for 10-14 d

Pediatric

Preterm neonate <7 days: 10 mg/kg PO/IV q12h
Term neonates to 12 years: 10 mg/kg PO/IV q8h
>12 years: Administer as in adults

Interactions

May cause hypertension when used concomitantly with adrenergic agents, including pseudoephedrine, sympathomimetic agents, and vasopressor or dopaminergic agents (reduce dose of dopamine or epinephrine if concurrent use required); serotonin syndrome may occur if used concomitantly with serotonergic agents, including TCAs, meperidine, dextromethorphan, trazodone, venlafaxine, and selective serotonin reuptake inhibitors; may cause myelosuppression or pseudomembranous colitis

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Has mild MAOI properties and has potential to have same interactions as other MAOIs; caution in uncontrolled hypertension, pheochromocytoma, carcinoid syndrome, or untreated hyperthyroidism, and patients who are at increased risk for bleeding, have preexisting thrombocytopenia, receive concomitant medications that may decrease platelet count or function, or who may require >2 wk of therapy (monitor platelet counts); unnecessary use may lead to development of resistance to drug; may cause peripheral or optic neuropathy

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Metronidazole (Flagyl, Protostat)

Imidazole ring-based antibiotic active against various anaerobic bacteria and protozoa. Used in combination with other antimicrobial agents (except for *C difficile* enterocolitis).
Not standard practice to use metronidazole alone because some anaerobic cocci and most microaerophilic streptococci are resistant. Use in combination with beta-lactam in treatment of anaerobic pneumonia and complicated pleuropulmonary infections.

Dosing

Adult

Loading dose: 15 mg/kg IV (or 1 g for 70-kg adult) over 1 h
Maintenance dose: 6 h following loading dose, infuse 7.5 mg/kg (or 500 mg for 70-kg adult) over 1 h q6-8h; not to exceed 4 g/d
Alternatively, 500 mg PO q6 - 8h X 7-14 d

Pediatric

Administer as in adults using body weight

Interactions

May increase toxicity of anticoagulants, cyclosporine, lithium, phenytoin, tacrolimus, and carbamazepine; cimetidine may increase toxicity; disulfiram reaction may occur with orally ingested ethanol; coadministration increases amiodarone toxicity (QT prolongation); increases disulfiram toxicity (psychotic symptoms) with concurrent use; phenobarbital and rifampin may increase metabolism of metronidazole

Contraindications

Documented hypersensitivity

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Caution with liver impairment, blood dyscrasias, and CNS disease; reduce dosage with severe hepatic disease; monitor for seizures and development of peripheral neuropathy

Fibrinolytic agents

Indicated for restoration of circulation through previously occluded vessels by dissolution of intraluminal thrombus or embolus not dissolved by the endogenous fibrinolytic system.

In pleuropulmonary infections, fibrinolytic activity and dissolution of fibrin strands increases drainage of pleural fluid, which, in turn, may facilitate resolution of the infection.

Alteplase (Activase)

Tissue plasminogen activator exerts effect on fibrinolytic system to convert plasminogen to plasmin. Plasmin degrades fibrin, fibrinogen, and procoagulant factors V and VIII. Serum half-life is 4-6 min but half-life lengthened when bound to fibrin in clot. Used in management of acute MI, acute ischemic stroke, and PE. Heparin and aspirin are not given for 24 h after tPA. Must be given within 3 h of stroke onset. Exclude hemorrhage by CT scan. If hypertensive, lower BP with labetalol, 10 mg IV. Safety and efficacy of concomitant administration with aspirin and heparin during first 24 h after onset of symptoms have not been investigated.

Dosing

Adult

25 mg in 100 mL 0.9% NaCl intrapleural instillation via chest tube once a day 3-5 d
Alternative regimen:
2 -4 mg mixed in 50 mL of diluent, injected through the chest tube, clamping tube for 2-4 h
Administered 1-3 times/d for 2-3 d
Both regimens have been reported to be successful in small patient series

Pediatric

4 mg in 40 mL of 0.9% NaCl intrapleural instillation via chest tube once a day for 3 d

Interactions

Anticoagulants and antiplatelets may increase risk of bleeding; may give heparin with and after alteplase infusions to reduce risk of rethrombosis; either heparin or alteplase may cause bleeding complications

Contraindications

Documented hypersensitivity; active internal bleeding, cerebrovascular accident, or stroke within last 2 mo, intracranial or intraspinal surgery or trauma, intracranial hemorrhage on pretreatment evaluation, suspicion of subarachnoid hemorrhage, intracranial neoplasm, arteriovenous malformation or aneurysm, bleeding diathesis, or severe uncontrolled hypertension

Precautions

Pregnancy

C - Fetal risk revealed in studies in animals but not established or not studied in humans; may use if benefits outweigh risk to fetus

Precautions

Monitor for bleeding, especially at arterial puncture sites, with coadministration of vitamin K antagonists; control and monitor blood pressure frequently during and following alteplase administration (when managing acute ischemic stroke); do not use >0.9 mg/kg to manage acute ischemic stroke; doses >0.9 mg/kg may cause ICH

Streptokinase (Kabikinase, Streptase)

Acts with plasminogen to convert plasminogen to plasmin. Plasmin degrades fibrin clots as well as fibrinogen and other plasma proteins. Increase in fibrinolytic activity that degrades fibrinogen levels for 24-36 h takes place with IV infusion of streptokinase. Absorbed from the pleural space.

Dosing

Adult

250,000 IU IV in 100 mL of NS qd or bid instilled into pleural space for 3-5 d

Pediatric

Not established

Interactions

Antifibrinolytic agents may decrease effects of streptokinase; heparin, warfarin, and aspirin may increase risk of bleeding

Contraindications

Documented hypersensitivity; active internal bleeding; intracranial neoplasm; aneurysm; diathesis; severe uncontrolled arterial hypertension

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Caution in severe hypertension, IM administration of medications, trauma, or surgery in previous 10 d; measure hematocrit, platelet count, aPTT, TT, PT, or fibrinogen levels before therapy is implemented; either TT or aPTT should be less than twice the reference range value following infusion of streptokinase and before instituting or reinstituting heparin; do not take BP in lower extremities because may dislodge a possible deep vein thrombus; PT, aPTT, TT, or fibrinogen should be monitored 4 h after initiation of therapy

Urokinase (Abbokinase)

Direct plasminogen activator that acts on endogenous fibrinolytic system and converts plasminogen to enzyme plasmin, which, in turn, degrades fibrin clots, fibrinogen, and other plasma proteins. Most often used for local fibrinolysis of thrombosed catheters and superficial vessels. Advantage is that agent is nonantigenic; however, more expensive than streptokinase, limiting use. When used for local fibrinolysis, urokinase is administered as local infusion directly into area of thrombus and with no bolus administered. Dose of medication should be adjusted to achieve clot lysis or patency of affected vessel.

Dosing

Adult

100,000 IU in 100 mL of NS qd or bid instilled into pleural space for 3-5 d

Pediatric

Not established

Interactions

Thrombolytic enzymes, alone or in combination with anticoagulants and antiplatelets, may increase risk of bleeding complications

Contraindications

Documented hypersensitivity; internal bleeding; recent trauma; history of intracranial or intraspinal surgery or trauma; stroke; intracranial neoplasm

Precautions

Pregnancy

B - Fetal risk not confirmed in studies in humans but has been shown in some studies in animals

Precautions

Caution in patients receiving IM administration of medications, severe hypertension, trauma, or surgery in previous 10 d; to avoid dislodging a possible deep vein thrombus, do not measure BP in lower extremities; monitor therapy by measuring PT, aPTT, TT, or fibrinogen approximately 4 h after initiation of therapy

Follow-up

Further Inpatient Care

- Patients require hospitalization for antibiotic therapy, drainage of pleural space, thrombolytic therapy (possibly), and surgery (in patients in whom medical therapy is unsuccessful).

Further Outpatient Care

- Often, prolonged antibiotic therapy is required, particularly in patients who have anaerobic infections. The length of antibiotic therapy is generally dictated by the response to antibiotics and clinical and radiologic resolution.

Inpatient & Outpatient Medications

- Extended treatment with antibiotics may be required. See Medication for the antibiotic list.

Transfer

- If specialty services are not available (interventional radiologist and/or thoracic surgeon), some patients may require transfer to a hospital that is able to provide these services.

Deterrence/Prevention

- Early diagnosis and intervention (thoracentesis and/or drainage procedure), may obviate the need for surgical treatment.

Complications

- Complications are related to adverse events related to incomplete drainage of infected pleural fluid. These include chronic, indolent infections, chest tube site infections, trapped lung, bronchopleural fistulas, and pneumothoraces.
- Untreated infections may lead to sepsis, septic shock, and death.

Prognosis

- Most patients recover, but the mortality rate remains approximately 10%.
- Appropriate antibiotic therapy and early drainage of pleural fluid are crucial for recovery.
- Approximately 15-25% of patients require surgical intervention, including decortication and/or an open drainage procedure.

Patient Education

- For excellent patient education resources, visit eMedicine's Lung and Airway Center. Also, see eMedicine's patient education article Bacterial Pneumonia.

Miscellaneous

Medicolegal Pitfalls

- Thoracentesis in patients with pneumonia and pleural effusions of sufficient size is mandatory to allow differentiation of uncomplicated from complicated pleural effusions or empyemas.
- The pleural fluid pH has the highest diagnostic accuracy in the assessment of uncomplicated or complicated pleural effusions.[27]
- Drainage procedures are essential in patients with complicated parapneumonic effusions to prevent adverse events associated with the infection.
- Indications for fibrinolytic and surgical treatment remain undefined. Consultation with a specialist is advised, and each patient should be managed on a case-by-case basis.

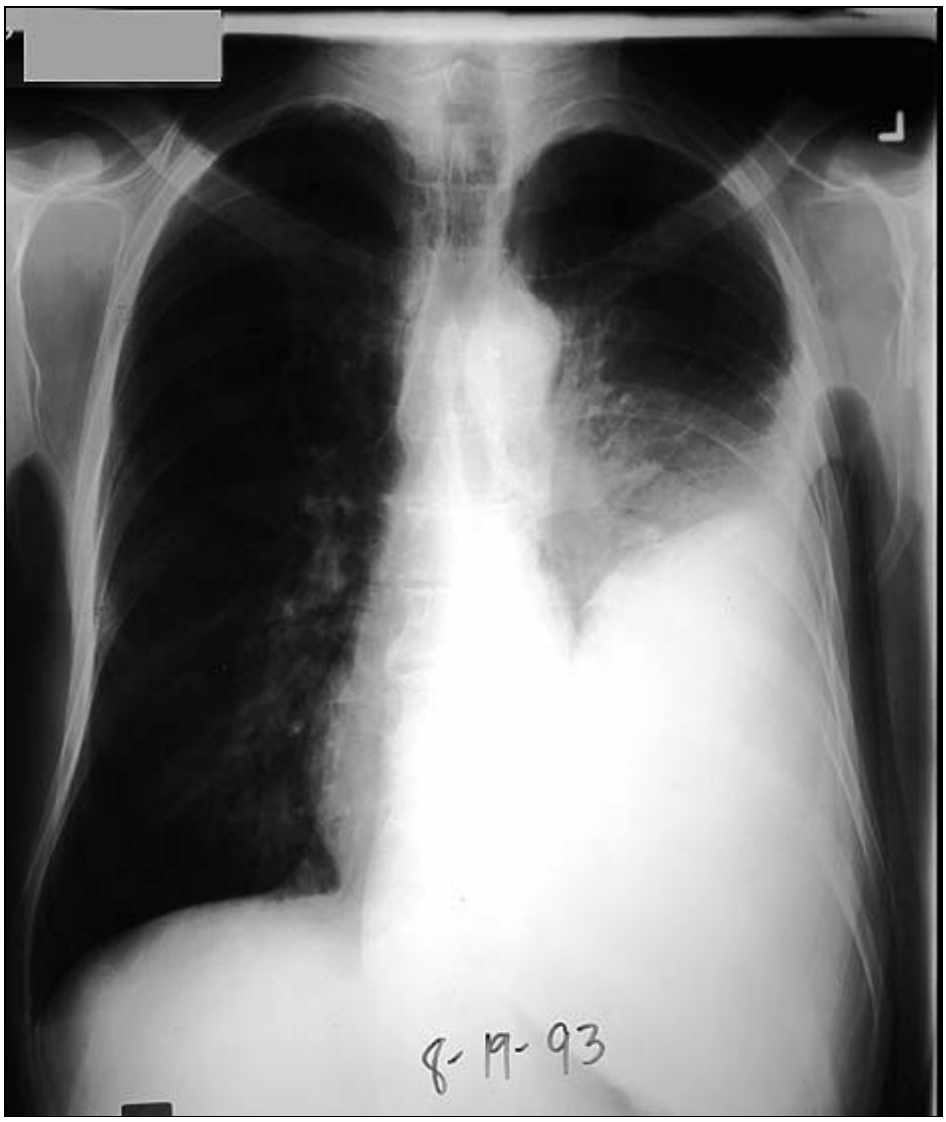
Special Concerns

- In patients with empyema and bronchopleural fistula, pleural fluid may drain internally and cause an overwhelming pneumonia. In patients who produce large amounts of sputum when in a specific position (eg, supine, decubitus), suspect a bronchopleural fistula.
    - Radiologically, a bronchopleural fistula is suggested by the presence of an air-fluid level in the pleural space. To differentiate the air-fluid level from the lung abscess, ultrasonography or CT scanning may be helpful.
    - The presence of bronchopleural fistula in conjunction with infected pleural fluid is a medical emergency. Immediately institute drainage, and promptly start appropriate antibiotics.
- An empyema distal to an obstructed bronchus such as an obstructing endobronchial carcinoma creates a unique management problem.
    - The underlying lung does not expand, but the empyema must be drained to control the infection. This results in either the need for a long-standing indwelling chest tube or an open chest wound for drainage. Patients require long-term antibiotics.
    - Radiation therapy or laser therapy of the affected bronchus may allow lung re-expansion.
- Postpneumonectomy empyemas account for approximately 25% of empyemas. The prevalence of postpneumonectomy empyema is 2-10%, and approximately half of these patients have bronchopleural or esophagopleural fistulas.
    - After a pneumonectomy, a characteristic evolution of radiologic findings develops. Deviations from this suggest the possibility of postpneumonectomy empyema.
    - In the postoperative period, if the volume of air increases or the mediastinum shifts toward the midline or

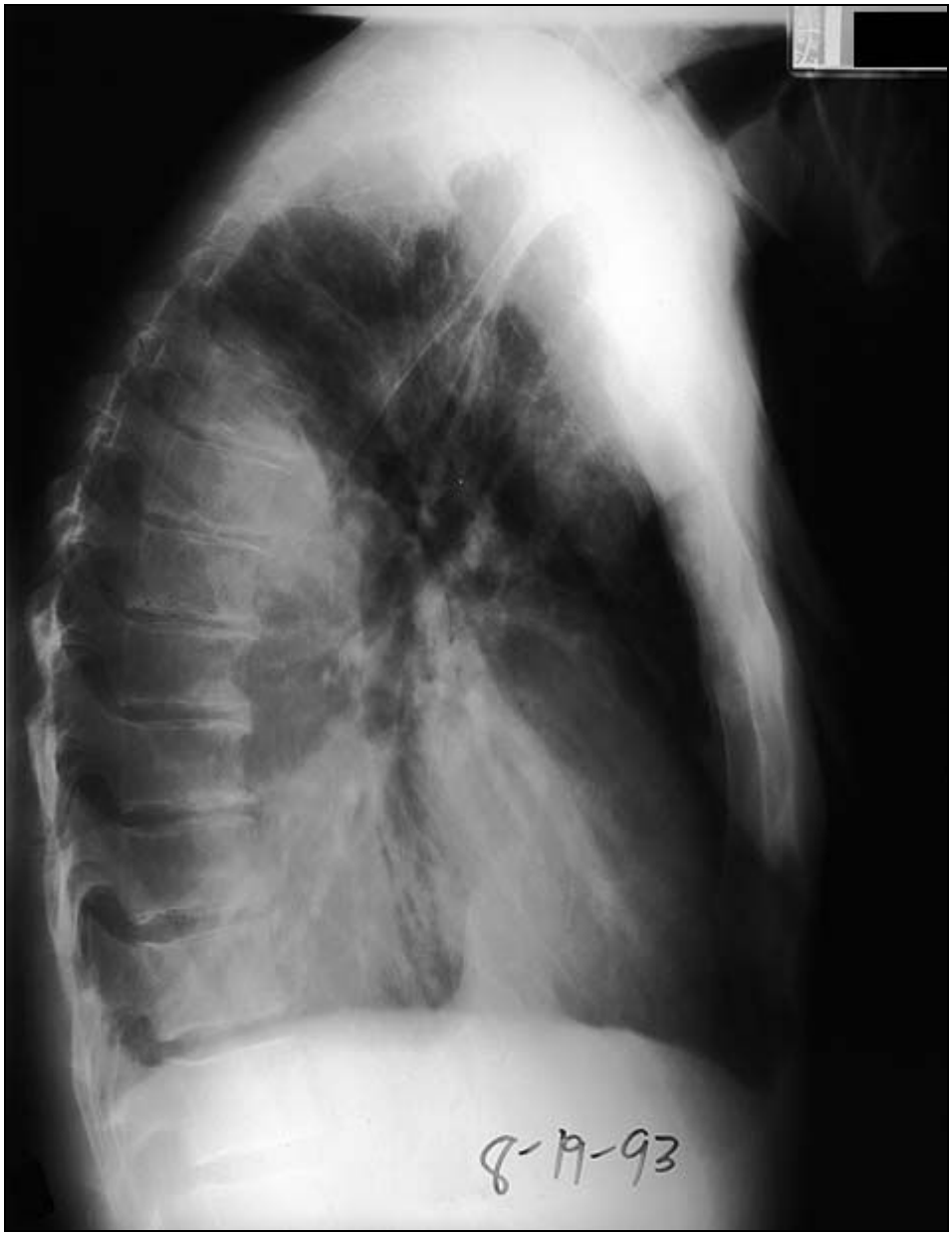
contralateral side, strongly consider postpneumonectomy empyema.

- Diagnosis is further established by thoracentesis demonstrating bacteria on the Gram stain of the pleural fluid. The usual bacteria responsible for infection are gram-negative organisms or *Staphylococcus aureus.*
- Treat all patients with postpneumonectomy empyema with a chest tube and appropriate antibiotics. If the patient does not have a bronchopleural fistula, antibiotic irrigation of the pleural space also appears to be effective in most patients.
- An alternate approach to postpneumonectomy empyema is the creation of a skin-lined fistula that allows drainage (and irrigation if desired) of pleural fluid. This is often referred to an Eloesser flap and permits outpatient management. Prolonged antibiotics are an essential component of treatment.
- A similar approach may be required to manage a persistent bronchopleural fistula. If surgical closure or the fistula is not possible, an Eloesser flap along with extended antibiotic therapy may be required.

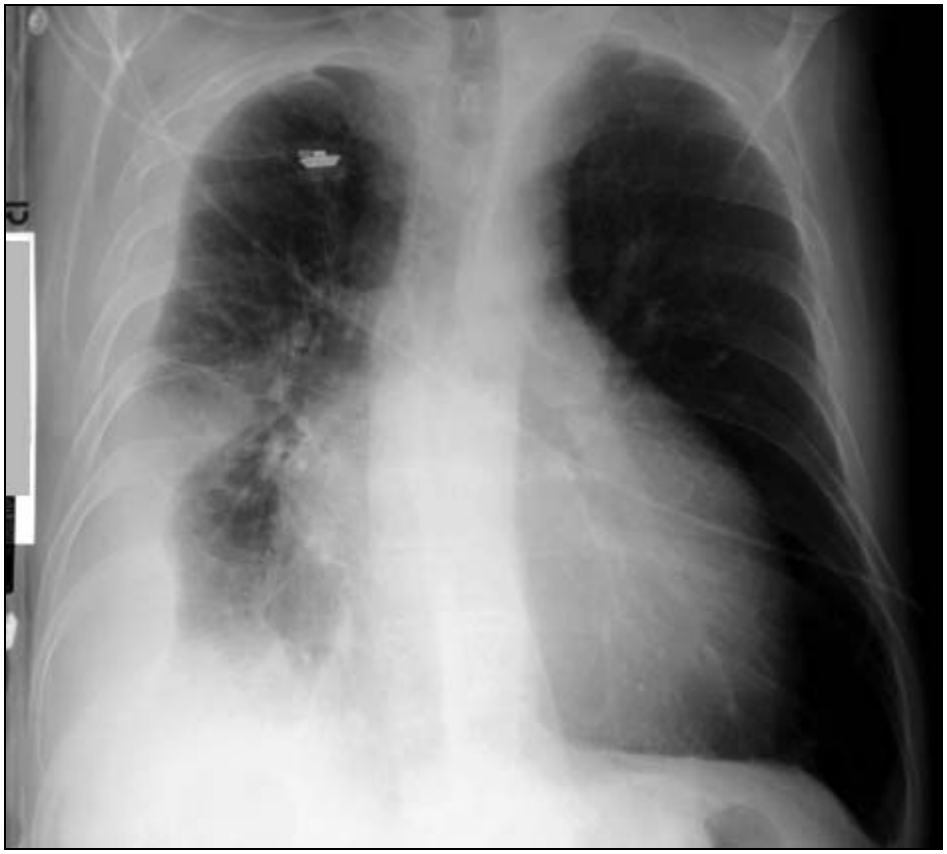
Multimedia



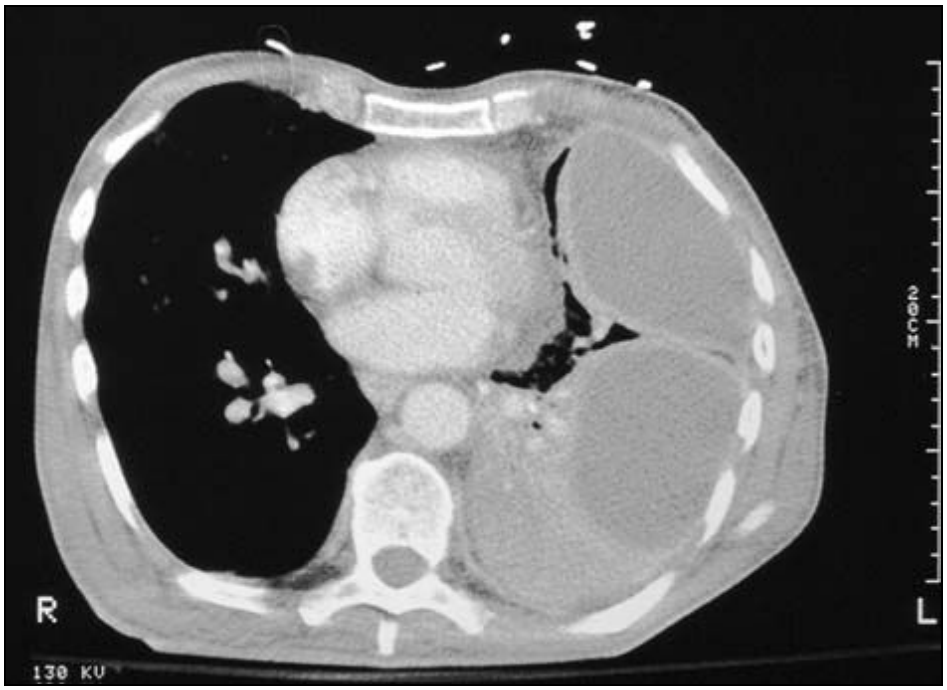
Media file 1: Left pleural effusion developed 4 days after antibiotic treatment for pneumococcal pneumonia. Patient developed fever, left-sided chest pain, and increasing dyspnea. During thoracentesis, purulent pleural fluid was removed, and the Gram stain showed gram-positive diplococci. The culture confirmed this to be Streptococcus pneumoniae.



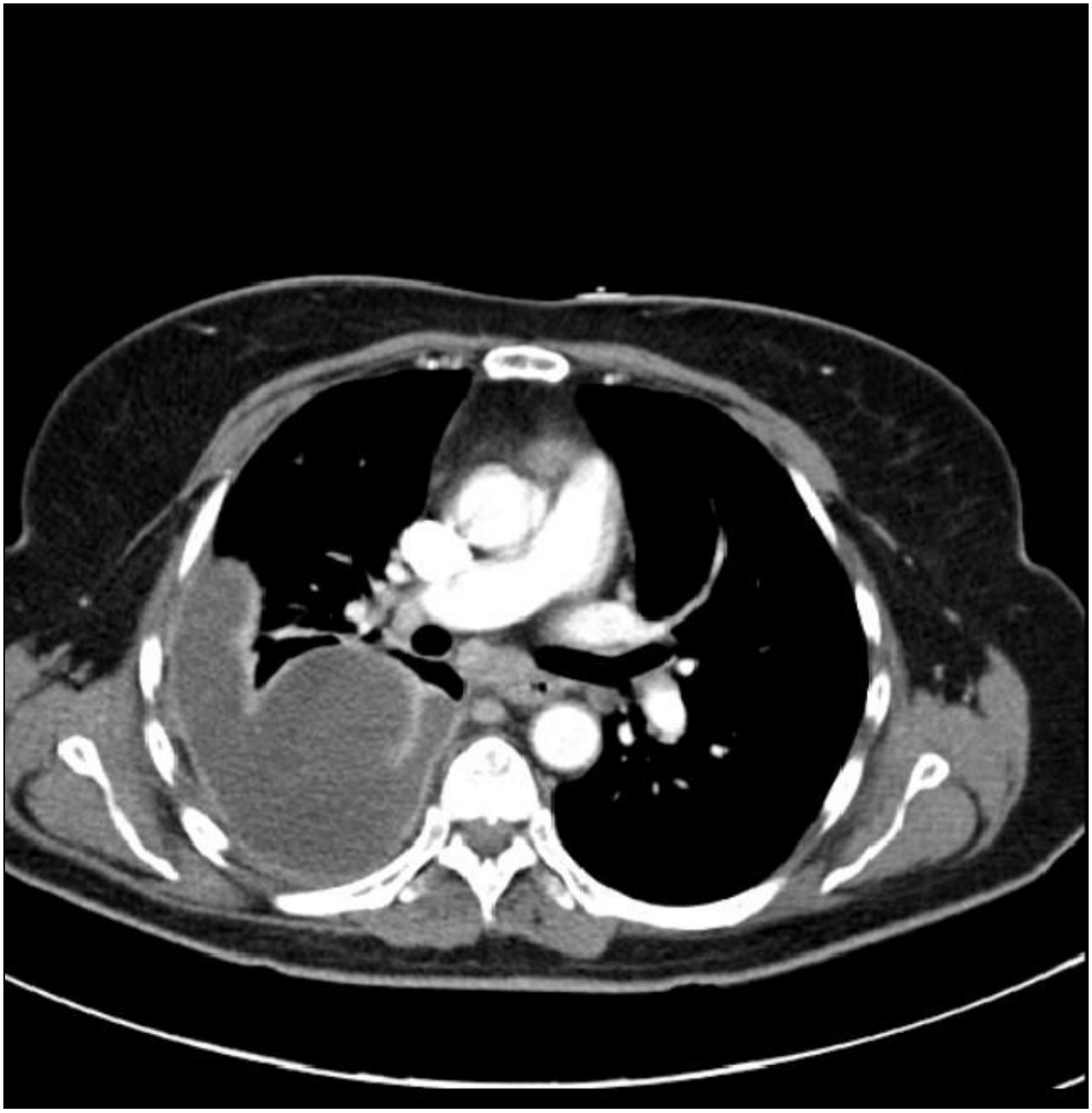
Media file 2: Left lateral chest radiograph shows a large, left pleural effusion.



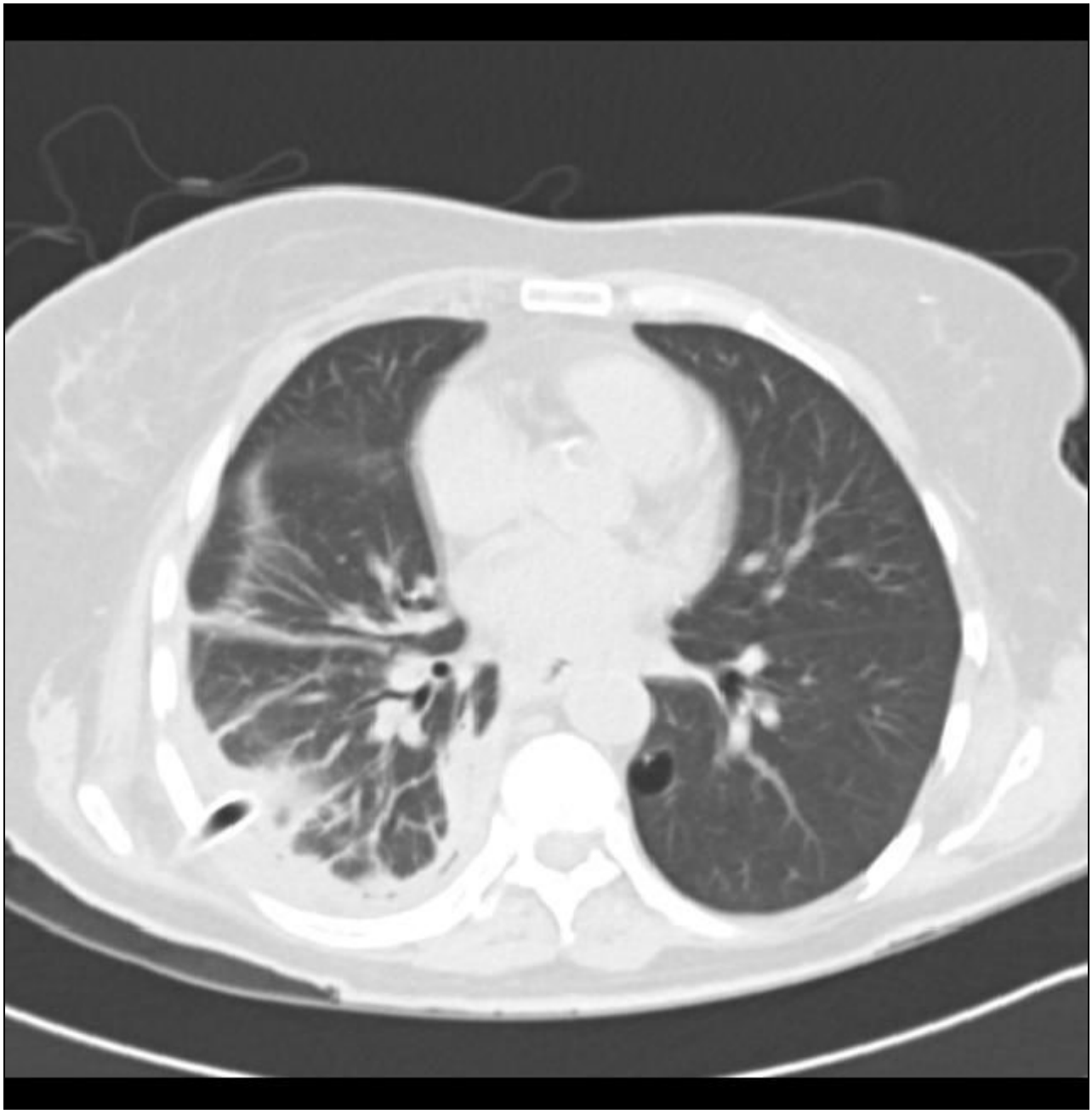
Media file 3: A right lateral decubitus chest radiograph shows a free-flowing pleural effusion, which should be sampled with thoracentesis for pH determination, Gram stain, and culture.



Media file 4: CT scan of thorax shows loculated pleural effusion on left and contrast enhancement of visceral pleura, indicating the etiology is likely an empyema.



Media file 5: Chest CT scan with intravenous contrast in a patient with mixed Streptococcus milleri and anaerobic empyema following aspiration pneumonia, showing a thickened contrast-enhanced pleural rind, high-density pleural effusion, loculation, and septation. Thoracentesis yielded foul-smelling pus.



Media file 6: Chest CT scan with intravenous contrast in a patient with mixed Streptococcus milleri and anaerobic empyema following aspiration pneumonia, 3 days following thoracostomy and intrapleural fibrinolysis (Reteplase).

References

1. Sahn SA. Diagnosis and management of parapneumonic effusions and empyema. *Clin Infect Dis*. Dec 1 2007;45(11):1480-6. [Medline].

2. Ahmed RA, Marrie TJ, Huang JQ. Thoracic empyema in patients with community-acquired pneumonia. *Am J Med*. Oct 2006;119(10):877-83. [Medline].

3. Tsang KY, Leung WS, Chan VL, Lin AW, Chu CM. Complicated parapneumonic effusion and empyema thoracis: microbiology and predictors of adverse outcomes. *Hong Kong Med J*. Jun 2007;13(3):178-86. [Medline].

4. Jerng JS, Hsueh PR, Teng LJ, Lee LN, Yang PC, Luh KT. Empyema thoracis and lung abscess caused by viridans streptococci. *Am J Respir Crit Care Med*. Nov 1997;156(5):1508-14. [Medline].

5. Bartlett JG, Gorbach SL, Thadepalli H, Finegold SM. Bacteriology of empyema. *Lancet*. Mar 2 1974;1(7853):338-40. [Medline].

6. Chalmers JD, Singanayagam A, Murray MP, Scally C, Fawzi A, Hill AT. Risk factors for complicated parapneumonic effusion and empyema on presentation to hospital with community-acquired pneumonia. *Thorax*. Jul 2009;64(7):592-7. [Medline].

7. [Guideline] Colice GL, Curtis A, Deslauriers J, et al. Medical and surgical treatment of parapneumonic effusions : an evidence-based guideline. *Chest*. Oct 2000;118(4):1158-71. [Medline].

8. [Guideline] Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis*. Mar 1 2007;44 Suppl 2:S27-72. [Medline].

9. [Guideline] Infectious Diseases Society of America/American Thoracic Society. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med*. Feb 15 2005;171(4):388-416. [Medline].

10. Davies CW, Lok S, Davies RJ. The systemic fibrinolytic activity of intrapleural streptokinase. *Am J Respir Crit Care Med*. Jan 1998;157(1):328-30. [Medline].

11. Davies RJ, Traill ZC, Gleeson FV. Randomised controlled trial of intrapleural streptokinase in community acquired pleural infection. *Thorax*. May 1997;52(5):416-21. [Medline].

12. Bouros D, Schiza S, Tzanakis N, Chalkiadakis G, Drositis J, Siafakas N. Intrapleural urokinase versus normal saline in the treatment of complicated parapneumonic effusions and empyema. A randomized, double-blind study. *Am J Respir Crit Care Med*. Jan 1999;159(1):37-42. [Medline].

13. Diacon AH, Theron J, Schuurmans MM, Van de Wal BW, Bolliger CT. Intrapleural streptokinase for empyema and complicated parapneumonic effusions. *Am J Respir Crit Care Med*. Jul 1 2004;170(1):49-53. [Medline].

14. Maskell NA, Davies CW, Nunn AJ, Hedley EL, Gleeson FV, Miller R. U.K. Controlled trial of intrapleural streptokinase for pleural infection. *N Engl J Med*. Mar 3 2005;352(9):865-74. [Medline].

15. Tokuda Y, Matsushima D, Stein GH, Miyagi S. Intrapleural fibrinolytic agents for empyema and complicated parapneumonic effusions: a meta-analysis. *Chest*. Mar 2006;129(3):783-90. [Medline].

16. Froudarakis ME, Kouliatsis G, Steiropoulos P, et al. Recombinant tissue plasminogen activator in the treatment of pleural infections in adults. *Respir Med*. Dec 2008;102(12):1694-700. [Medline].

17. Levinson GM, Pennington DW. Intrapleural fibrinolytics combined with image-guided chest tube drainage for pleural infection. *Mayo Clin Proc*. Apr 2007;82(4):407-13. [Medline].

18. Cameron R, Davies HR. Intra-pleural fibrinolytic therapy versus conservative management in the treatment of adult parapneumonic effusions and empyema. *Cochrane Database Syst Rev*. Apr 16 2008;CD002312. [Medline].

19. Luh SP, Chou MC, Wang LS, Chen JY, Tsai TP. Video-assisted thoracoscopic surgery in the treatment of complicated parapneumonic effusions or empyemas: outcome of 234 patients. *Chest*. Apr 2005;127(4):1427-32. [Medline].

20. Hope WW, Bolton WD, Stephenson JE. The utility and timing of surgical intervention for parapneumonic empyema in the era of video-assisted thoracoscopy. *Am Surg*. Jun 2005;71(6):512-4. [Medline].

21. Casali C, Storelli ES, Di Prima E, Morandi U. Long-term functional results after surgical treatment of parapneumonic thoracic empyema. *Interact Cardiovasc Thorac Surg*. Jul 2009;9(1):74-8. [Medline].

22. Potaris K, Mihos P, Gakidis I, Chatziantoniou C. Video-thoracoscopic and open surgical management of thoracic empyema. *Surg Infect (Larchmt)*. Oct 2007;8(5):511-7. [Medline].

23. Chan DT, Sihoe AD, Chan S, et al. Surgical treatment for empyema thoracis: is video-assisted thoracic surgery "better" than thoracotomy?. *Ann Thorac Surg*. Jul 2007;84(1):225-31. [Medline].

24. Wang ZT, Wang LM, Li S, Jian H. Electronic endoscope insertion into a thoracic drainage tube is a new technique in the treatment and diagnosis of pleural diseases. *Surg Endosc*. Jul 2009;23(7):1671-3. [Medline].

25. St Peter SD, Tsao K, Harrison C, et al. Thoracoscopic decortication vs tube thoracostomy with fibrinolysis for empyema in children: a prospective, randomized trial. *J Pediatr Surg*. Jan 2009;44(1):106-11; discussion 111. [Medline].

26. Ng CS, Wan S, Lee TW, Wan IY, Arifi AA, Yim AP. Post-pneumonectomy empyema: current management strategies. *ANZ J Surg*. Jul 2005;75(7):597-602. [Medline].

27. Heffner JE, Brown LK, Barbieri C, DeLeo JM. Pleural fluid chemical analysis in parapneumonic effusions. A meta-analysis. *Am J Respir Crit Care Med*. Jun 1995;151(6):1700-8. [Medline].

Keywords

empyema thoracis, pleural effusions, pleural effusion, parapneumonic pleural effusion, pleuropulmonary empyema, complicated parapneumonic pleural effusion, *Staphylococcus aureus, S aureus, Streptococcus pneumoniae, S pneumoniae, Streptococcus milleri, S milleri, Klebsiella, Pseudomonas, Haemophilus, Bacteroides, Peptostreptococcus,* uncomplicated parapneumonic effusion, thoracic empyema, thoracoplasty, decortication, pneumonia, parapneumonic effusion, esophageal perforation, trauma, surgical procedure on pleural space, septicemia

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Disclosure: Nothing to disclose.

Acknowledgments

The authors and editors of eMedicine gratefully acknowledge the contributions of previous author, Sat Sharma, MD, FRCPC, to the development and writing of this article.

Further Reading