

# BMJ Best Practice

## Empyema

Straight to the point of care



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# Table of Contents

<b>Overview</b>	<b>3</b>
Summary	3
Definition	3
<b>Theory</b>	<b>4</b>
Epidemiology	4
Etiology	4
Pathophysiology	5
Classification	5
Case history	6
<b>Diagnosis</b>	<b>8</b>
Approach	8
History and exam	14
Risk factors	15
Investigations	17
Differentials	23
Criteria	24
<b>Management</b>	<b>25</b>
Approach	25
Treatment algorithm overview	30
Treatment algorithm	32
Secondary prevention	49
Patient discussions	49
<b>Follow up</b>	<b>50</b>
Monitoring	50
Complications	51
Prognosis	52
<b>Guidelines</b>	<b>54</b>
Diagnostic guidelines	54
Treatment guidelines	54
<b>References</b>	<b>55</b>
<b>Images</b>	<b>61</b>
<b>Disclaimer</b>	<b>65</b>

## Summary

Empyema is defined as the presence of pus in the pleural space.

Risk factors include pneumonia, iatrogenic intervention in the pleural space, diabetes, and alcohol abuse.

In patients with symptoms and signs of infection and a significant pleural effusion, thoracentesis (pleural aspiration) must be performed urgently.

If empyema or a complicated parapneumonic effusion is diagnosed, a chest drain must be inserted urgently.

A prolonged course of antibiotics is also required.

If patients do not improve with antibiotics and drainage of the pleural space, surgery or intrapleural enzyme therapy should be considered.

Mortality is approximately 15% to 20%.

## Definition

Empyema is defined as the presence of frank pus in the pleural space. Parapneumonic effusions are effusions caused by an underlying pneumonia. A simple parapneumonic effusion is not infected, whereas a complicated parapneumonic effusion develops once infection has spread to the pleural space. These three conditions represent a spectrum of pleural inflammation in response to infection, ranging from a simple parapneumonic effusion to empyema.

## Epidemiology

More than 65,000 people develop pleural infections in the US and UK combined each year.[4] One study of working-age adults in the US found an overall incidence rate of community-acquired pneumonia of 10.6 in 1000 person-years.[5] Another study found that the incidence of nonventilator hospital-acquired pneumonia in the US is 3.63 in 1000 patient-days.[6] Parapneumonic effusions may be caused by either community-acquired or hospital-acquired pneumonia. Between 20% and 57% of the 1 million patients hospitalized each year in the US with pneumonia develop a parapneumonic effusion.[7] Approximately 5% to 10% of parapneumonic effusions develop into empyemas.[8] There is some evidence that empyema is increasing in incidence in both adults and children, the reason for which is unknown.[9] [10] [11] [12] [13] [14]

Empyema is more common in men, with a male to female ratio of approximately 2:1. It also has a bimodal age distribution, occurring more in the sixth or seventh decade of life and in young children.[14] The incidence of parapneumonic effusion and empyema is approximately 3.3 in 100,000 children per year, and there is some evidence that this figure is increasing.[15] [16]

## Etiology

Empyema represents the most severe end of the spectrum of pleural inflammation in response to infection.[1] Initially, inflammation of the pleural space leads to a simple, free-flowing parapneumonic effusion. In most cases, this resolves with antibiotic treatment, but approximately 7% become infected, leading to the development of a complicated parapneumonic effusion (CPE).[17] If the CPE is undertreated, an empyema may form.

The majority of pleural infections follow bacterial pneumonia.[8] Pleural inflammation leads to the development of a parapneumonic effusion and invasion of the pleural space by bacteria. Therefore, risk factors for pneumonia, including aspiration (e.g., following a stroke, in the presence of a nasogastric or endotracheal tube), presence of an immunocompromised state (e.g., due to hematologic disease, chemotherapy, HIV, or malnutrition), alcohol abuse, and intravenous drug use are also risk factors for empyema. Other causes of empyema include bronchogenic carcinoma, esophageal rupture, blunt or penetrating chest trauma, mediastinitis with pleural extension, infected congenital cysts of the airway and esophagus, extension from sources below the diaphragm, cervical and thoracic spine infections, and postsurgical etiologies.[8] Less common causes include subphrenic abscesses, extensions of mediastinal or chest wall infections, and bacteremia.

Although empyema usually develops following pneumonia, the microbiology of empyema differs from that of pneumonia. Empyema is frequently polymicrobial, and an organism is only identified in approximately 60% of pleural infections.[18] The organisms cultured in empyema following community-acquired pneumonia are significantly different from those which develop following hospital-acquired pneumonia or iatrogenic etiologies. In community-acquired infection, gram-positive aerobic bacteria are most common, particularly the *Streptococcus milleri* group, *Streptococcus pneumoniae*, and staphylococci.[18] The latter is particularly prominent in the pediatric population, where 87% of infections are caused by aerobic gram-positive cocci.[19] Gram-negative bacteria are less commonly cultured in community-acquired infection, but anaerobes are often seen both in isolation and coinfection with aerobic organisms, although they are difficult to culture so may be involved in a greater percentage of cases.[8] [18] In hospital-acquired infection, staphylococci (particularly MRSA) are the most commonly cultured pathogen, though there has also been an emergence of gram-negative bacteremia.[18] [20] Due to this, different antibiotics should be used in patients with

community- and hospital-acquired infections, and broader-spectrum antibiotics are required for the empirical treatment of empyema than those used in the treatment of pneumonia.[8]

## Pathophysiology

Empyema represents the end-stage of a progressive process evolving from a small amount of free-flowing, noninfected pleural fluid to a large amount of frank pus that can become loculated and result in thick pleural peel.

The formation of empyema is classically divided into 3 stages: exudative stage, fibrinopurulent stage, and organizational stage. During the exudative stage (Stage 1), sterile pleural fluid accumulates in the pleural space secondary to inflammation and increased permeability of the visceral pleura. The fibrinopurulent stage (Stage 2) commences with bacterial invasion of the pleural space and is characterized by the deposition of fibrin on visceral and parietal pleural membranes and the formation of fibrinous septae, loculations, and adhesions. The high metabolic activity leads to a fall in pleural fluid glucose concentration and pH, and neutrophil lysis leads to an increase in lactate dehydrogenase levels. If the infection progresses, the empyema becomes organized (Stage 3), with the formation of thick, nonelastic pleural peel and dense fibrinous septations that inhibit lung expansion as a result of fibroblast proliferation, causing a condition known as trapped lung.[21]

## Classification

### American College of Chest Physicians[1]

Parapneumonic effusions are subdivided into 4 categories.

Category 1: Simple parapneumonic effusion

- Small free-flowing pleural effusion.

Category 2: Simple parapneumonic effusion

- Small to moderate (i.e., less than half of the hemithorax) free-flowing effusion
- Gram stain and culture of the pleural fluid negative, pleural fluid pH >7.2, and glucose >60 mg/dL.

Category 3: Complicated parapneumonic effusion (must have at least one of the following)

- Size of effusion: more than half of the hemithorax, loculated or associated with a thickened parietal pleura
- Gram stain or culture positive
- Pleural fluid pH <7.2 or glucose <60 mg/dL.

Category 4: Empyema

- Pus present in the pleural space.

### Light's classification of pleural effusions[2]

Class 1: Nonsignificant



- Thickness of the fluid on the decubitus chest x-ray <10 mm.

Class 2: Typical parapneumonic

- Thickness of the fluid on the decubitus chest x-ray >10 mm, pleural fluid pH >7.2, and glucose >40 mg/dL.

Class 3: Borderline complicated

- Pleural fluid pH 7.0 to 7.2 or LDH >1000 IU/L, Gram stain and culture negative.

Class 4: Simple complicated

- Pleural fluid pH <7.0, Gram stain or culture positive, not loculated, no frank pus present.

Class 5: Complex complicated

- Pleural fluid pH <7.0, Gram stain or culture positive, multiple loculated.

Class 6: Simple empyema

- Presence of frank pus, single locule, or free-flowing effusion.

Class 7: Complex empyema

- Presence of frank pus and multiple loculations.

## Community- versus hospital-acquired empyema<sup>[3]</sup>

Community-acquired empyema

- Empyema that develops following community-acquired pneumonia.

Hospital-acquired empyema

- Empyema following hospital-acquired pneumonia, surgery, or iatrogenic intervention in the pleural space.

## Case history

### Case history #1

A 65-year-old man re-presents to his physician, following treatment for pneumonia, with fever, increasing breathlessness, and right-sided chest pain. He feels lethargic and has lost 4 kg in weight. He initially presented 3 weeks earlier with a productive cough and breathlessness. At that time, he was diagnosed with community-acquired pneumonia and treated with a course of oral antibiotics. He has a past medical history of poorly controlled type 2 diabetes mellitus. On examination, he is septic, with a temperature of 101.3°F (38.5°C), BP 90/60 mmHg, pulse rate 110 beats/minute, and respiratory rate 28 breaths/minute. He has dullness to percussion and decreased breath sounds at the right lung base. Chest radiograph demonstrates a loculated right pleural effusion, which is confirmed on point-of-care ultrasound. Laboratory examination reveals WBC count  $20 \times 10^9/L$ . He undergoes ultrasound-guided thoracentesis (pleural aspiration) that shows a septated pleural effusion, and frank pus is aspirated.

## Other presentations

Empyema may present following iatrogenic intervention in the pleural space, thoracic surgery, thoracic trauma, hospital-acquired pneumonia, or de novo in a patient without a history of pneumonia. Immunocompromised patients, or patients who are already taking antibiotics, may present with few clinical signs of infection. Patients with anaerobic empyemas can present with a more indolent illness characterized by weight loss, constitutional upset, and fatigue.

## Approach

All patients presenting with evidence of infection and respiratory symptoms should undergo investigation for a parapneumonic effusion, especially those who fail to improve despite antibiotic treatment for pneumonia.[2]

The initial test of choice is a chest radiograph, and if the clinician is skilled with point-of-care ultrasound (POCUS) then this can also be used to help quantify and qualify the effusion.[8] If a significant effusion is seen, a diagnostic thoracentesis (pleural aspiration) with ultrasound guidance is required.[8] In patients where a complicated parapneumonic effusion or empyema is suspected, it is reasonable to pursue tube thoracostomy up front to help achieve source control and provide an avenue for continuous drainage and possible instillation of therapeutics.[8] Aspiration of frank pus is diagnostic of empyema, but if this is not present, further biochemical and microbiological tests are required to diagnose whether or not a parapneumonic effusion is complicated.

## Clinical history

### Presenting symptoms

- The key presenting symptoms of empyema are breathlessness (secondary to large pleural effusion or pneumonia), fever, and pleuritic chest pain (pain worsened by deep breathing, coughing, sneezing, and chest movement). Other associated symptoms include those of pneumonia (productive cough, green or rust-colored sputum, shortness of breath) and systemic infection (anorexia, malaise, fatigue, rigors).
- Patients tend to have a subacute history of illness, with a mean duration of symptoms before admission of 2 weeks.[23] [24] Failure of patients with pneumonia to respond to antibiotics or a deterioration in clinical condition suggests the development of a complicated parapneumonic effusion or empyema.
- The lack of characteristic clinical signs can delay diagnosis. Immunocompromised patients or patients who are already taking antibiotics may present with few clinical signs of infection. Patients with anaerobic empyemas can present with a more indolent illness characterized by weight loss, constitutional upset, and fatigue.

### Past medical history

- The majority of patients who develop empyema have a recent history of pneumonia, thoracic trauma, or iatrogenic intervention in the pleural space such as thoracic surgery, or medical procedures such as chest drain insertion (4%), thoracentesis (pleural aspiration), tube thoracostomy (chest drain insertion), and aspiration of pneumothoraces or pleural effusions.[3]
- Patients may have a history of a medical condition predisposing them to the development of pneumonia and hence empyema, such as pre-existing lung diseases (e.g., bronchiectasis, COPD, lung cancer) or conditions associated with an increased risk of aspiration (e.g., stroke, presence of a nasogastric or endotracheal tube). Immunocompromised patients (e.g., due to hematologic disease, chemotherapy, HIV, or malnutrition) are also at increased risk of developing empyema.

### Social history

- Alcohol abuse and drug addiction are additional risk factors for the development of empyema.



## Clinical exam

Examination reveals evidence of a pleural effusion with or without signs of systemic infection.

- Large pleural effusions are characterized by dullness on percussion (classically described as "stony" in quality) and diminished breath sounds with reduced vocal resonance on the affected side. Smaller pleural effusions may not be detectable on clinical exam.
- Septic shock presents with pyrexia, tachypnea, tachycardia, and hypotension (BP <90/60). Such patients require urgent resuscitation.

## Blood tests

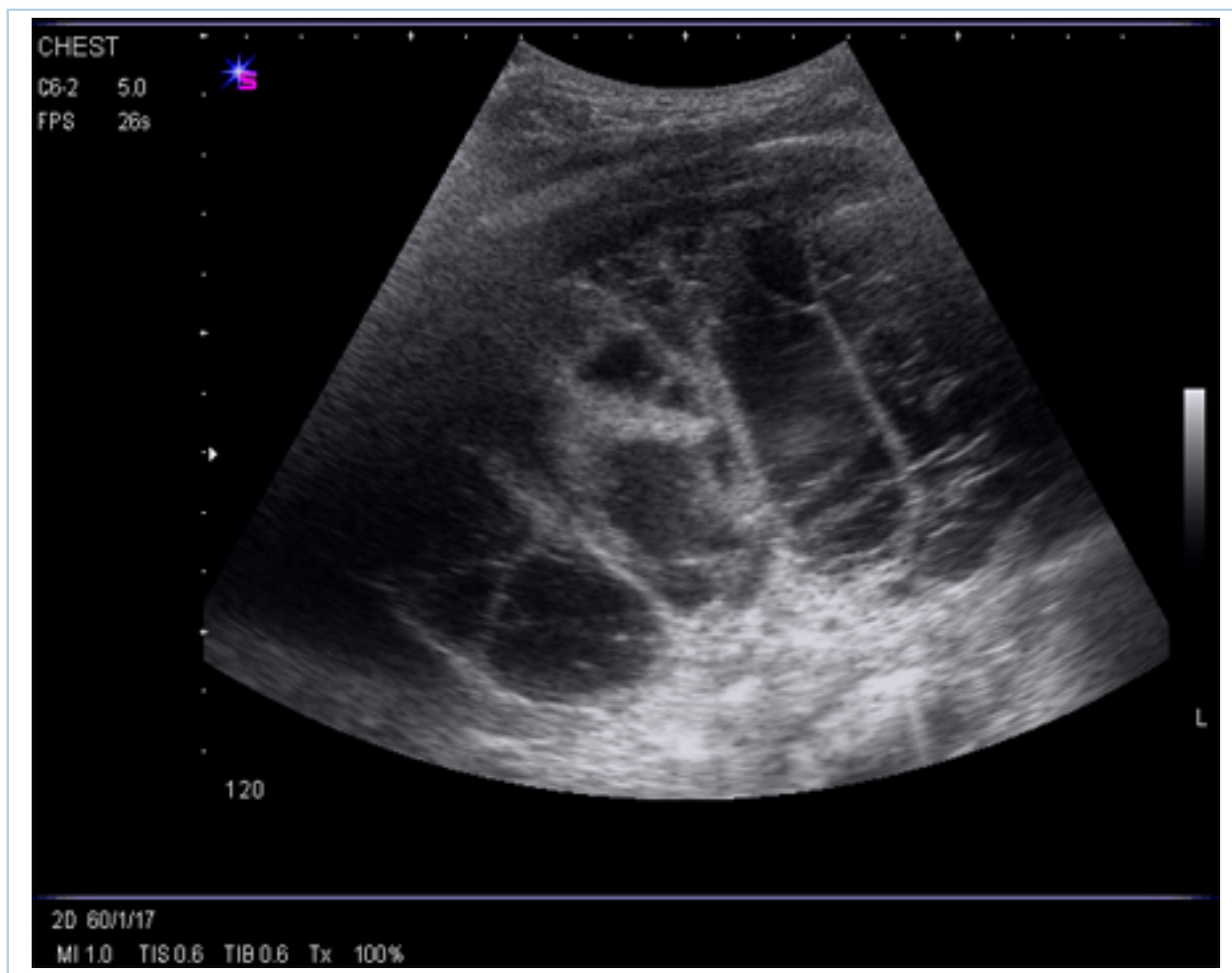
A complete blood count, C-reactive protein (CRP), and blood cultures should be undertaken in all patients with suspected empyema at presentation.<sup>[8]</sup> In empyema, the white blood cell count and the CRP will be raised as part of a systemic response to infection. Blood cultures may be positive for specific pathogens even if the pleural fluid culture is negative. Ideally, blood cultures should be taken before the initiation of antibiotics if the clinical state of the patient permits. Additionally, a basic metabolic panel including albumin and renal function tests can be obtained in order to help prognosticate patients at high risk for a poor outcome, using the RAPID (Renal [urea], Age, fluid Purulence, Infection source, Dietary [albumin]) clinical score.<sup>[18] [25]</sup>

## Initial imaging studies

The initial investigations of choice are chest x-ray and thoracic ultrasound, and should be undertaken in all patients with a suspected empyema at presentation.<sup>[8]</sup> Chest computed tomography (CT) should be reserved for complicated cases (e.g., children that fail to respond to treatment, or if there is doubt about the diagnosis).<sup>[26] [27]</sup>

An urgent chest x-ray (CXR) should be organized in all patients who present with respiratory symptoms and evidence of sepsis, as it can demonstrate the presence of a pleural effusion. A lateral decubitus CXR is more sensitive than a posteroanterior view for detecting an effusion, but its use has been superseded by thoracic ultrasound given the ease of rapid use and ubiquitous nature of ultrasound. The presence of a loculated effusion suggests an empyema. Empyemas may have a pleurally based "D"-shaped appearance which can be mistaken for a lung mass. There may be associated pulmonary consolidation due to pneumonia and, in ventilated supine patients, a pleural effusion will appear as a diffuse unilateral increase in opacification. An effusion measuring >10 mm on a lateral decubitus CXR, in association with evidence of infection, requires thoracentesis (pleural aspiration).<sup>[1]</sup>

Thoracic ultrasound is more sensitive than a CXR for the detection of pleural effusions.<sup>[8]</sup> Features suggestive of an empyema on thoracic ultrasound include the presence of echogenic fluid, loculations, and septations, as shown below.<sup>[28]</sup>



*Ultrasound image of heavily septated empyema*

*From the collection of Najib Rahman, RTU, Oxford*

As empyemas are often associated with a raised hemidiaphragm or tethered lung, image guidance decreases complication rate substantially and so is preferred for all procedures. The use of ultrasound to guide thoracentesis (pleural aspiration) in order to reduce its associated complication rate is advised.<sup>[29]</sup> Ultrasonography is also recommended to guide chest drain insertion, especially in small or loculated effusions.<sup>[8]</sup>

## Thoracentesis

All patients with evidence of infection and a significant pleural effusion should undergo thoracentesis (pleural aspiration) with ultrasound guidance.<sup>[1] [8][30]</sup>

Aspiration of frank pus is diagnostic of an empyema and no other investigations are required to establish the diagnosis, with the exception of pleural fluid microbiology to guide antibiotic therapy. If the aspirate does not reveal frank pus, further analysis is required to assess whether it is a complicated parapneumonic effusion. This involves measurement of the pleural fluid pH, total protein concentration, lactate dehydrogenase (LDH) level, glucose concentration, and white cell differential.

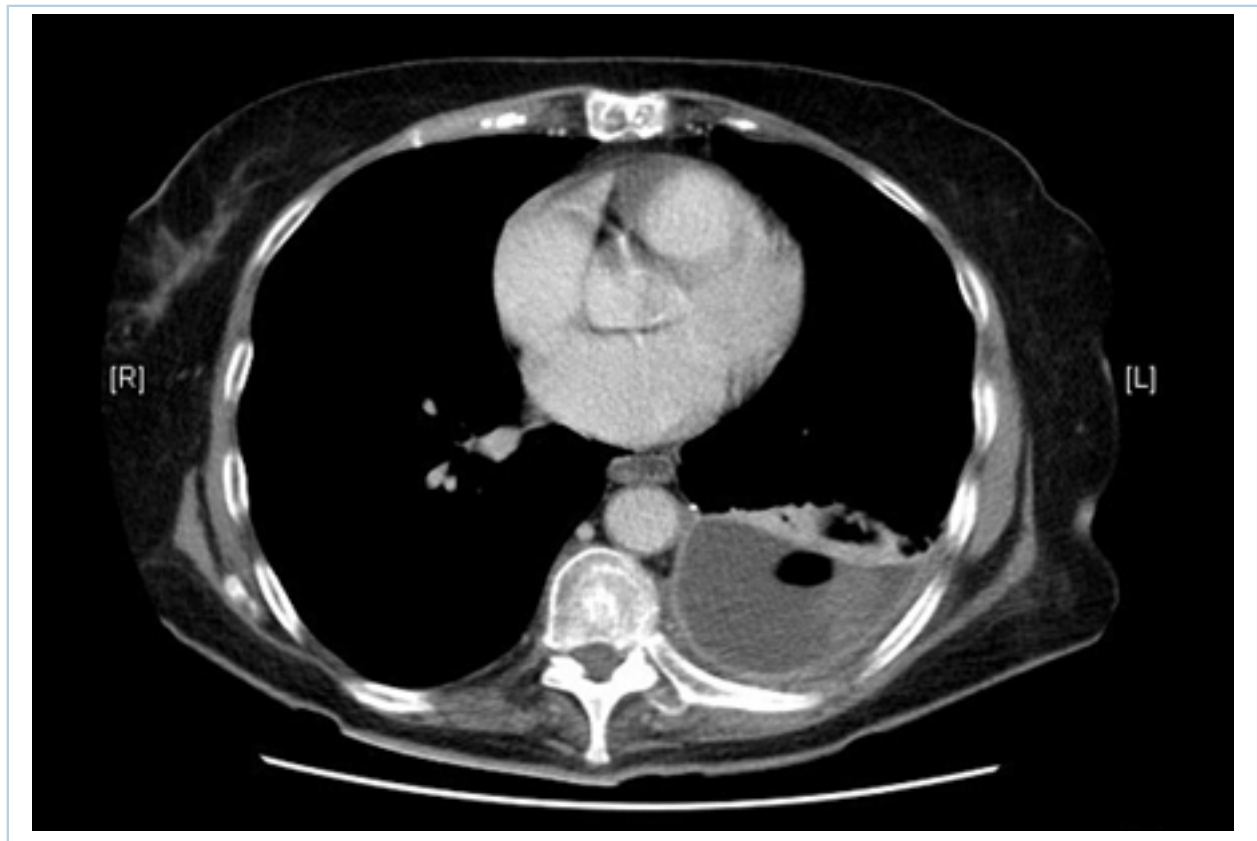
All samples should be sent for microscopy, culture, and sensitivity testing. Cytology may be used in cases where the diagnosis is unclear (e.g., for the detection of malignant cells in a malignant pleural effusion).

- Pleural fluid appearance: Empyema is characterized by frank pus. Complicated parapneumonic effusions may be serous or cloudy. Use caution when interpreting fluid appearance, as infection can be present even in simple appearing fluid.
- Pleural fluid odor: Putrid odor is suggestive of an anaerobic infection.
- Pleural fluid pH: Samples should be stored anaerobically.[31] Local anesthetics can falsely lower the pH. Physicians should have access to a blood gas analyzer so that samples can be tested immediately to enable immediate insertion of a chest drain if indicated. If the sample is frank pus, the pH should not be tested as it can damage the analyzer.
- Pleural fluid total protein concentration: If frank pus is aspirated, the protein concentration does not require analysis.[8] [18]
- Pleural fluid LDH level: If frank pus is aspirated, the LDH level does not require analysis.
- Pleural fluid glucose concentration: If frank pus is aspirated, glucose does not require analysis. If an accurate pleural fluid pH is not available, low glucose levels can be used as an alternative predictor of a complicated parapneumonic effusion requiring urgent chest drain insertion. Pleural fluid glucose has been shown to be a robust predictor in this circumstance.[32]
- Pleural fluid white cell differential: Polymorphonuclear leukocytes are the predominating (>90%) cell type. The predominance of lymphocytes in the exudate raises the suspicion of tuberculosis or malignancy.
- Pleural fluid microscopy, culture, and sensitivity: A positive Gram stain or culture is obtained in 60% to 70% of samples.[23] This can be used to guide antibiotic treatment.

## Further imaging studies

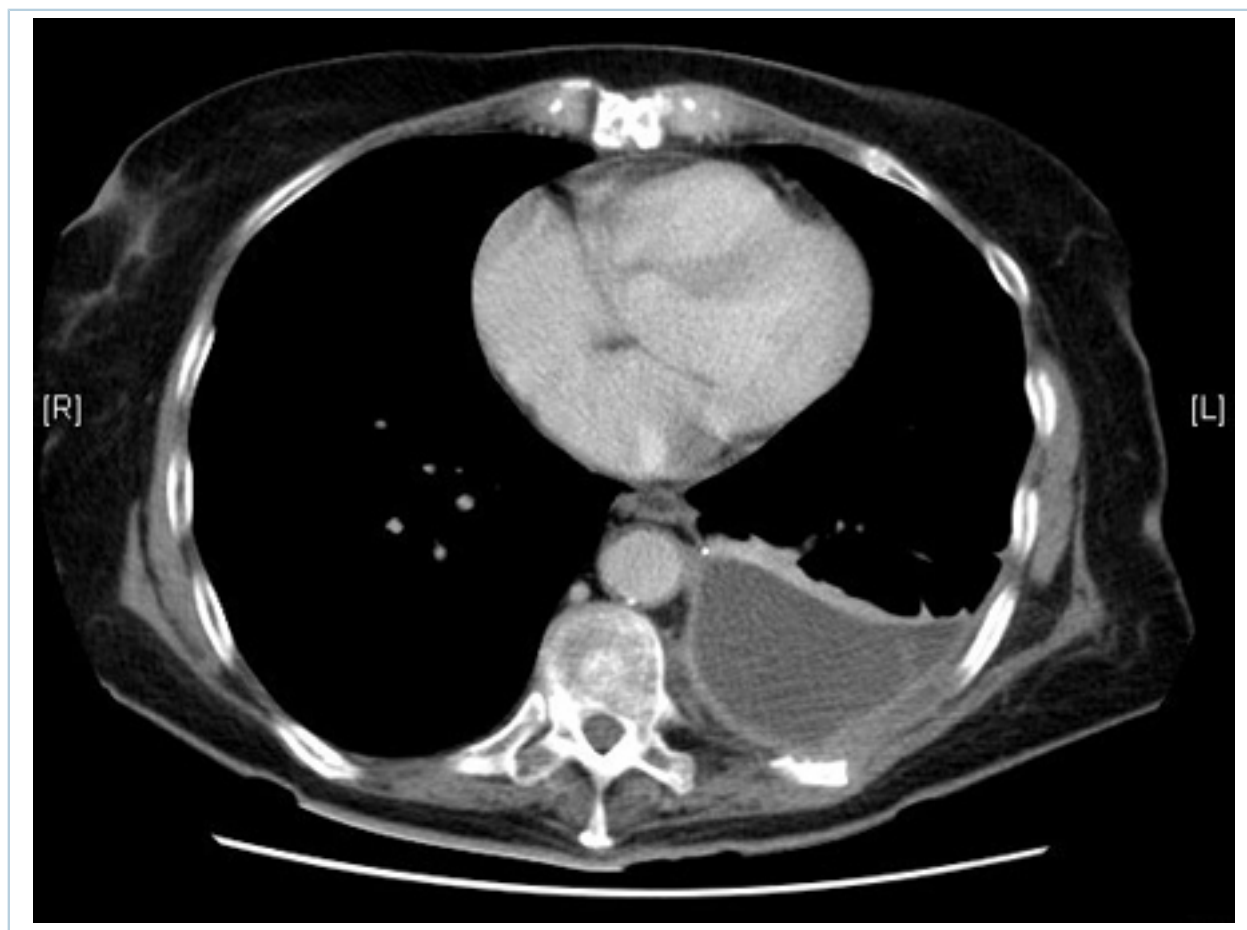
Further imaging studies are performed when there is doubt about the diagnosis or to confirm the correct position of the chest drain.[8]

Contrast-enhanced thoracic CT can help to distinguish empyema from other pleural effusions and lung abscesses, and should be done with tissue phase contrast.[33]



*CT scan of thoracic empyema*

*From the collection of Najib Rahman, RTU, Oxford*

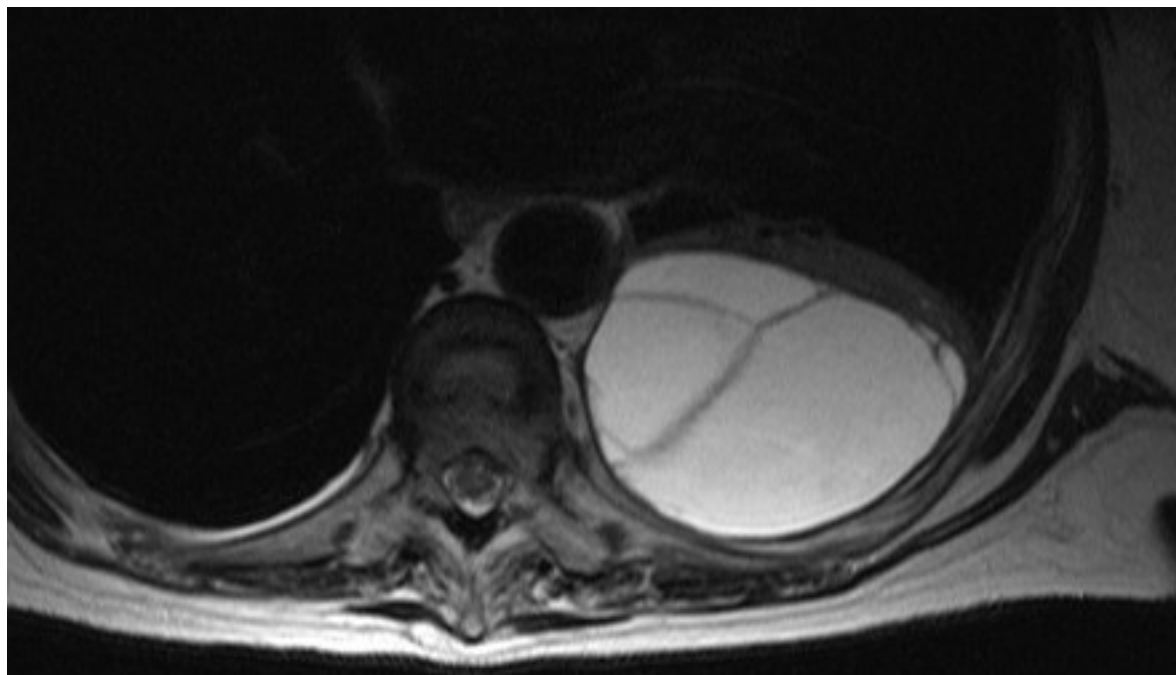


*CT scan of thoracic empyema*

*From the collection of Najib Rahman, RTU, Oxford*

Enhancement of the pleura with contrast is characteristic of empyema. The split pleura sign represents enhancement of the visceral and parietal pleura with interposed fluid. Pleural thickening may be visible, but this is also seen in malignancy; therefore, using pretest probability of malignancy can help guide initial therapy. Contrast-enhanced thoracic CT is especially useful for confirmation of the correct positioning of the chest drain and may help in the planning of surgery.

Magnetic resonance imaging is unable to accurately diagnose an empyema and is not routinely performed in the diagnosis or management of empyema. It is generally reserved for patients who are unable to undergo contrast-enhanced CT.<sup>[34]</sup> It may show septations, loculated pleural fluid, or chest wall invasion.



*MRI scan of septated empyema*  
 From the collection of Najib Rahman, RTU, Oxford

A positron emission tomography scan is another possible imaging technique, but its use is limited by the fact that it is unable to distinguish between malignancy and empyema.<sup>[35]</sup> It is generally not performed in the diagnosis or management of empyema.<sup>[8]</sup>

As the causative organism in 40% of pleural infections remains unidentified, pleural fluid polymerase chain reaction may aid pathogen identification, allowing specific antibiotics to be chosen.<sup>[23]</sup> However, further prospective evidence is required on this technique before it can be routinely recommended.

## History and exam

### Key diagnostic factors

#### recent pneumonia (common)

- Failure of patients with pneumonia to respond to antibiotics, or a deterioration in clinical condition, suggests the development of a complicated parapneumonic effusion or empyema.

#### constitutional symptoms (common)

- Malaise, anorexia, weight loss, or fatigue may occur.

#### pyrexia and rigors (common)

- Signs of pneumonia, empyema, and systemic infection.

#### dullness to percussion (common)

- Dullness occurs at the lung base in pleural effusions and pneumonia, but that associated with an effusion is classically described as "stony" in quality.



**reduced breath sounds and reduced vocal resonance (common)**

- Decreased air entry is found in pleural effusions and pneumonia.

**signs of sepsis (common)**

- Evidence of sepsis includes pyrexia, tachypnea, tachycardia, and hypotension (BP <90/60). Such patients require urgent resuscitation.

**Other diagnostic factors****subacute presentation (common)**

- Patients usually present with a 1 to 2 week history of symptoms.

**productive cough (common)**

- A cough productive of green or rust-colored sputum may be present in pneumonia.

**pleuritic chest pain (common)**

- Chest pain on inspiration results from inflammation of the parietal pleura (the visceral pleura is not innervated).

**dyspnea (common)**

- Presence of a large pleural effusion can cause breathlessness.
- The patient may also be breathless if there is associated pneumonia.

**recent instrumentation of the pleural space (common)**

- Patients who have had recent surgery, tunneled pleural catheter placement, or other manipulation or trauma of their pleural space are considered high risk.

## Risk factors

**Strong****pneumonia**

- The majority of empyemas develop following bacterial pneumonia.<sup>[8]</sup> Pleural inflammation leads to the development of a parapneumonic effusion and invasion of the pleural space by bacteria.
- Therefore, risk factors for pneumonia, including aspiration (e.g., following a stroke, in the presence of a nasogastric or endotracheal tube), immunocompromise, alcohol abuse, and drug addiction are also risk factors for empyema.
- Patients who fail to respond to antibiotic treatment for pneumonia should be reassessed for development of an empyema.

**iatrogenic interventions in the pleural space**

- Iatrogenic empyemas can occur following intervention in the pleural space such as thoracic surgery or medical procedures such as chest drain insertion, thoracentesis (pleural aspiration), tube thoracostomy (chest drain insertion), and aspiration of pneumothoraces or pleural effusions.<sup>[22]</sup>

**thoracic trauma**

- Blunt or penetrating chest trauma can lead to empyema.[\[22\]](#)
- Undrained hemothoraces can become secondarily infected, resulting in empyema.

**immunocompromised state**

- Patients immunocompromised due to hematologic disease, chemotherapy, HIV, or malnutrition are at increased risk of developing empyema.
- The lack of characteristic clinical signs can delay diagnosis.

**comorbid lung disease**

- Pre-existing lung diseases, such as bronchiectasis, COPD, and lung cancer increase the risk of developing empyema by contributing to reduced lung clearance.
- Patients with comorbidities are also at increased risk of dying from an empyema.[\[3\]](#)

**Weak****male sex**

- The male to female ratio of patients with empyema is approximately 2:1.[\[23\]](#)

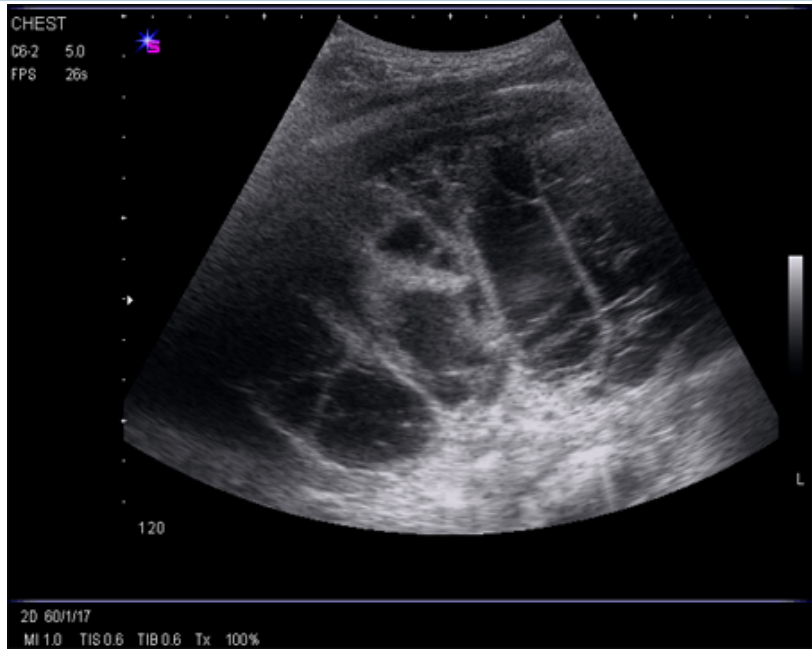
**older or young age**

- Empyema is more common in older people and young children. Adults tend to present in the sixth or seventh decade.[\[23\]](#) The incidence of parapneumonic effusion and empyema is approximately 3.3 in 100,000 children per year,[\[15\]](#) and there is some evidence that this figure is increasing.[\[16\]](#)

# Investigations

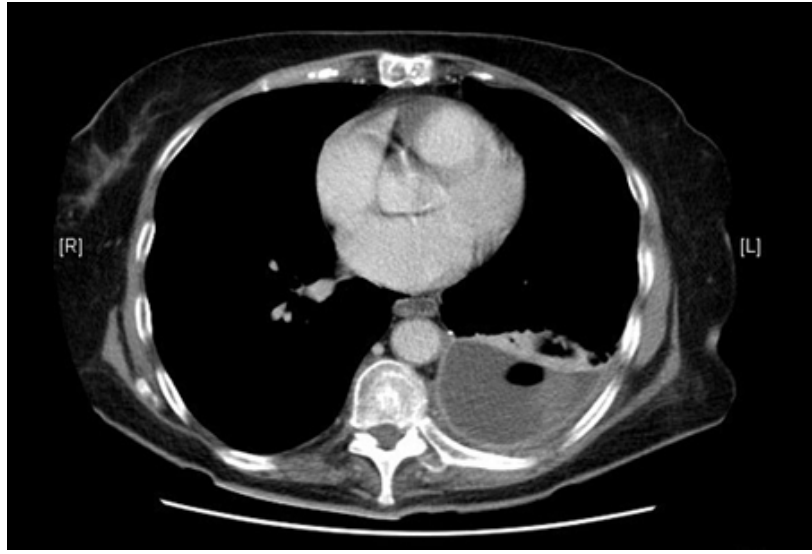
## 1st test to order

Test	Result
<b>blood cultures</b> <ul style="list-style-type: none"> <li>Blood cultures may be positive even if the pleural fluid culture is negative.</li> <li>Should be taken before the initiation of antibiotics if the clinical state of the patient permits.</li> </ul>	<b>positive for specific pathogens</b>
<b>CRP</b> <ul style="list-style-type: none"> <li>Part of a systemic response to infection.</li> </ul>	<b>elevated</b>
<b>WBC count</b> <ul style="list-style-type: none"> <li>Part of a systemic response to infection.</li> </ul>	<b>elevated</b>
<b>metabolic panel</b> <ul style="list-style-type: none"> <li>To include albumin and renal function tests. These help prognosticate patients that are at high risk for a poor outcome, using the RAPID (Renal [urea], Age, fluid Purulence, Infection source, Dietary [albumin]) clinical score.[25]</li> </ul>	<b>varies</b>
<b>chest x-ray</b> <ul style="list-style-type: none"> <li>An urgent CXR should be scheduled in all patients who present with respiratory symptoms and evidence of sepsis.</li> <li>Can demonstrate the presence of a pleural effusion.[8] A lateral decubitus CXR is more sensitive than a posteroanterior view for detecting an effusion, but its use has been superseded by thoracic ultrasound given the ease of rapid use and ubiquitous nature of ultrasound.</li> <li>The presence of a loculated effusion suggests an empyema. Empyemas may have a pleurally based, "D"-shaped appearance which can be mistaken for a lung mass.</li> <li>In ventilated supine patients, a pleural effusion will appear as a diffuse unilateral increase in opacification.</li> <li>There may be associated pulmonary consolidation due to pneumonia.</li> <li>An effusion measuring &gt;10 mm on a lateral decubitus CXR, in association with evidence of infection, requires thoracentesis (pleural aspiration).[1]</li> </ul>	<b>blunting of costophrenic angle or effusion on affected side, possible consolidation, pleurally based "D" shape in empyema</b>
<b>thoracic ultrasound</b> <ul style="list-style-type: none"> <li>More sensitive than a CXR for the detection of pleural effusions.[8]</li> <li>Features suggestive of an empyema on ultrasound include the presence of echogenic fluid, loculations, and septations, as shown below.[28]</li> </ul>	<b>presence of a pleural effusion which may be echogenic, loculated, and/or septated</b>

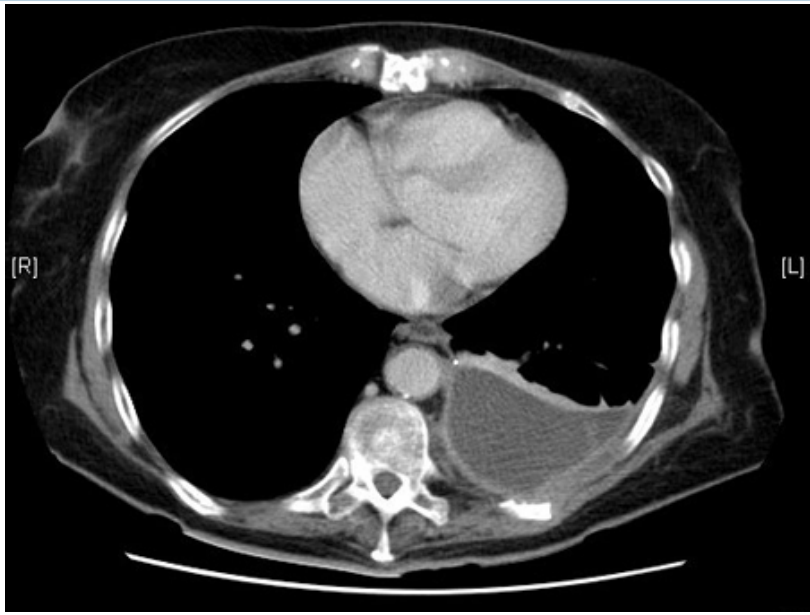
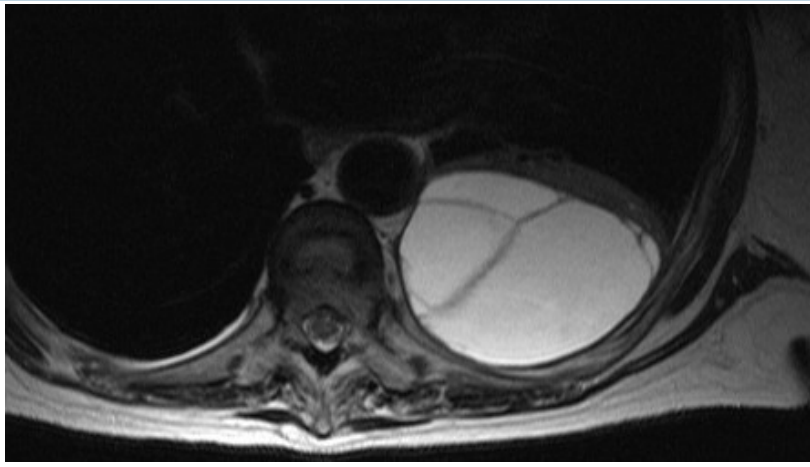
Test	Result
 <p><i>Ultrasound image of heavily septated empyema</i> From the collection of Najib Rahman, RTU, Oxford</p> <ul style="list-style-type: none"> <li>• Empyemas are often associated with a raised hemidiaphragm or tethered lung; therefore, image guidance decreases complication rate substantially and so is preferred for all procedures.</li> <li>• The use of ultrasound to guide thoracentesis in order to reduce its associated complication rate is advised.<a href="#">[29]</a></li> <li>• Ultrasonography is also recommended to guide chest drain insertion, especially in small or loculated effusions.<a href="#">[8]</a></li> </ul>	
<b>thoracentesis: pleural fluid appearance</b> <ul style="list-style-type: none"> <li>• Aspiration of frank pus is diagnostic of an empyema, and no other investigations are required to establish the diagnosis.</li> </ul>	<b>frank pus in empyema, serous or cloudy in complicated parapneumonic effusions</b>
<b>thoracentesis: pleural fluid odor</b> <ul style="list-style-type: none"> <li>• Putrid odor is suggestive of an anaerobic infection.</li> </ul>	<b>putrid in anaerobic infection</b>
<b>thoracentesis: pleural fluid pH</b> <ul style="list-style-type: none"> <li>• Samples should be stored anaerobically.<a href="#">[31]</a> Local anesthetics can falsely lower the pH. Physicians should have access to a blood gas analyzer so that samples can be tested immediately to enable immediate insertion of a chest drain if indicated. If the sample is frank pus, the pH should not be tested as it can damage the analyzer.</li> </ul>	<b>&lt;7.2</b>
<b>thoracentesis: pleural fluid total protein concentration</b> <ul style="list-style-type: none"> <li>• If frank pus is aspirated, the protein concentration does not require analysis.</li> </ul>	<b>&gt;30 g/dL</b>
<b>thoracentesis: pleural fluid LDH level</b> <ul style="list-style-type: none"> <li>• If frank pus is aspirated, the LDH level does not require analysis.</li> </ul>	<b>&gt;2-3 times above upper limit of normal range for serum</b>
<b>thoracentesis: pleural fluid glucose concentration</b> <ul style="list-style-type: none"> <li>• If frank pus is aspirated, glucose does not require analysis. If an accurate pleural fluid pH is not available, low glucose levels can be</li> </ul>	<b>&lt;60 mg/dL (&lt;3.3 mmol/L)</b>

Test	Result
used as an alternative predictor of a complicated parapneumonic effusion requiring urgent chest drain insertion. Pleural fluid glucose has been shown to be a robust predictor in this circumstance. <a href="#">[32]</a>	
<b>thoracentesis: pleural fluid white cell differential</b> <ul style="list-style-type: none"> <li>The predominance of lymphocytes in the exudate raises the suspicion of tuberculosis or malignancy.</li> </ul>	<b>predominance of polymorphonuclear leukocytes (&gt;90%)</b>
<b>thoracentesis: pleural fluid microscopy, culture, and sensitivity</b> <ul style="list-style-type: none"> <li>A positive Gram stain or culture is obtained in 60% to 70% of samples.<a href="#">[23]</a> This can be used to guide antibiotic treatment.</li> </ul>	<b>Gram stain or culture positive</b>

Other tests to consider

Test	Result
<div><p><b>contrast-enhanced thoracic CT</b></p><ul style="list-style-type: none"><li>• Chest CT should be reserved for complicated cases (e.g., children that fail to respond to treatment, or if there is doubt about the diagnosis).[26] [27]</li><li>• Done with tissue phase contrast.</li></ul></div> <div></div> <div><p><i>CT scan of thoracic empyema</i> <i>From the collection of Najib Rahman, RTU, Oxford</i></p></div>	<p><b>lenticular pleural effusion causing compression of adjacent lung, "split pleura sign," thickened pleura, loculations, septations, or gas bubbles, possible adjacent pneumonia</b></p>



Test	Result
<div data-bbox="233 185 1046 797">  </div> <div data-bbox="368 817 912 875"> <p><i>CT scan of thoracic empyema</i> From the collection of Najib Rahman, RTU, Oxford</p> </div> <ul style="list-style-type: none"> <li>• Can help distinguish empyema from other pleural effusions and lung abscesses.[33]</li> <li>• Enhancement of the pleura with contrast is characteristic of empyema.</li> <li>• Pleural thickening may be visible, but is also seen in malignancy.</li> <li>• The split pleura sign represents enhancement of the visceral and parietal pleura with interposed fluid.</li> <li>• Useful for confirmation of correct chest tube placement and to assess for source control and clearance of the pleural space. It may also help in the planning of surgery.</li> </ul>	
<p><b>MRI of thorax</b></p> <ul style="list-style-type: none"> <li>• An MRI is unable to accurately diagnose an empyema and is not routinely performed in the diagnosis or management of empyema. It is generally reserved for patients who are unable to undergo contrast-enhanced CT. It may show septations, loculated pleural fluid, or chest wall invasion.[34]</li> </ul> <div data-bbox="233 1462 1046 1926">  </div> <div data-bbox="368 1944 912 2002"> <p><i>MRI scan of septated empyema</i> From the collection of Najib Rahman, RTU, Oxford</p> </div>	<p><b>septations, loculated pleural fluid, chest wall invasion</b></p>

Test	Result
<b>PET scan</b> <ul style="list-style-type: none"><li>A PET scan is another possible imaging technique, but its use is limited by the fact that it is unable to distinguish between malignancy and empyema.[35] It is generally not performed in the diagnosis or management of empyema.</li></ul>	<b>fluorodeoxyglucose avid</b>
<b>pleural fluid polymerase chain reaction (PCR)</b> <ul style="list-style-type: none"><li>As the causative organism in 40% of pleural infections remains unidentified, PCR may aid pathogen identification, allowing specific antibiotics to be chosen.[23]</li><li>Further prospective evidence is required on this technique.</li></ul>	<b>positive PCR for specific pathogens</b>

## Differentials

Condition	Differentiating signs / symptoms	Differentiating tests
<b>Pneumonia</b>	<ul style="list-style-type: none"> <li>No differentiating signs or symptoms.</li> </ul>	<ul style="list-style-type: none"> <li>CXR: consolidation without associated effusion.</li> </ul>
<b>Uncomplicated parapneumonic effusion</b>	<ul style="list-style-type: none"> <li>No differentiating signs or symptoms.</li> </ul>	<ul style="list-style-type: none"> <li>Pleural fluid: serous in appearance.</li> <li>Gram stain and culture: negative.</li> <li>Pleural fluid pH: &gt;7.2.[1]</li> </ul>
<b>Lung abscess</b>	<ul style="list-style-type: none"> <li>Cough productive of foul-smelling sputum.</li> </ul>	<ul style="list-style-type: none"> <li>CXR: cavitating lung lesion with air-fluid level.</li> <li>Contrast-enhanced thoracic CT: demonstrates thick-walled irregular cavity with indistinct boundary between abscess and normal lung, vessels may be visible passing through the abscess.[33]</li> </ul>
<b>Malignant pleural effusion</b>	<ul style="list-style-type: none"> <li>Longer history of symptoms.</li> <li>Past medical history of cancer which may be known to be metastatic.</li> <li>Caution is required as malignancy and infected pleural effusions can coexist.</li> </ul>	<ul style="list-style-type: none"> <li>Pleural fluid pH in both malignant and infected effusions: &lt;7.2.</li> <li>Thoracentesis pleural fluid cytology: may demonstrate malignant cells.</li> <li>CXR: may demonstrate primary tumor.</li> <li>Thoracic ultrasound: may demonstrate pleural thickening and nodularity.</li> <li>CT scan: findings suggestive of malignant pleural effusion are pleural thickening extending onto the mediastinum, circumferential pleural thickening, nodularity, and pleural thickening &gt;1 cm.</li> </ul>
<b>Chylothorax</b>	<ul style="list-style-type: none"> <li>No infective symptoms.</li> </ul>	<ul style="list-style-type: none"> <li>Pleural fluid: remains milky in appearance when centrifuged, in empyema debris settles out on centrifuge.</li> <li>Pleural fluid: triglycerides &gt;110 mg/dL, levels of 50 to 110 mg/dL should be followed by lipoprotein analysis for the detection of chylomicrons.</li> </ul>

Condition	Differentiating signs / symptoms	Differentiating tests
<b>Esophageal rupture</b>	<ul style="list-style-type: none"> <li>Recent history of vomiting or retching.</li> </ul>	<ul style="list-style-type: none"> <li>Pleural fluid: contains food debris and amylase of salivary origin.</li> <li>CXR: may show hydropneumothorax.</li> <li>CT scan: may demonstrate esophageal wall thickening, mediastinal widening, and a pleural space gas-liquid level.</li> <li>Oral contrast-enhanced CT: may show contrast within the mediastinum.</li> <li>Esophagram with gastrograffin: reveals the location of rupture. An empyema can often develop secondary to the esophagram.</li> </ul>
<b>Hemothorax</b>	<ul style="list-style-type: none"> <li>History of anticoagulation or bleeding diathesis.</li> <li>Close temporal relationship with thoracic trauma or iatrogenic intervention in the pleural space.</li> <li>Caution is required as a hemothorax may become secondarily infected.</li> </ul>	<ul style="list-style-type: none"> <li>Pleural fluid: frankly bloody.</li> <li>Pleural fluid hematocrit: &gt;50% of peripheral blood hematocrit.</li> </ul>

## Criteria

### Development of empyema in association with pneumonia<sup>[22]</sup>

#### Stage 1

- Parapneumonic effusion (free-flowing exudate): low white cell count, lactate dehydrogenase (LDH) level less than half that in the serum, normal pH and glucose levels, no bacterial organisms.

#### Stage 2

- Fibrinopurulent (bacterial invasion across the damaged lung epithelium with immune response): pH <7.2, glucose <40 mg/dL (<2.2 mmol/L), LDH >1000 IU/L. Called empyema if frank pus is found.

#### Stage 3

- Chronic organizing (scar tissue formation): a fibrous pleural cortex begins to form, which may encase the lung, preventing re-expansion, impairing lung function, and creating a persistent pleural space with continuing potential for infection.

## Approach

All patients with empyema and complicated parapneumonic effusion require antibiotic therapy and urgent pleural fluid drainage.[1] [8][36] The key goal of therapy is sterilization of the pleural space.

Patients may be septic at presentation and require emergency fluid resuscitation and urgent intravenous antibiotics even before the diagnosis is established. Standard initial medical management also includes tube thoracostomy with continuous drainage of the infected pleural space.[37] The largest multicenter prospective observational study (PILOT) demonstrates that this standard therapy fails in over 30% of cases.[38]

In patients who fail to respond to chest tube drainage and antibiotics, either intrapleural enzyme therapy and/or surgery should be considered.[18] Patients should be under the care of a respiratory physician or thoracic surgeon.

One Cochrane review found no statistically significant difference in mortality between primary surgical and nonsurgical management of pleural empyema for all age groups.[39] Although video-assisted thoracoscopic surgery (VATS) reduced the length of hospital stay compared with thoracostomy drainage alone, there was insufficient evidence about the impact of fibrinolytic therapy.[39] As of November 2023, there has yet to be a randomized controlled trial comparing intrapleural enzyme therapy to early surgery, although a feasibility study was recently published (MIST-3), and set the framework for future evaluation.[37]

## Adults

Initial antibiotic therapy[8]

- All adults should initially receive empirical intravenous antibiotics based on local microbiology guidelines to cover the likely causative organisms, both aerobic and anaerobic. Clinicians should keep in mind differences between community-acquired and hospital-acquired pathogens.
- Penicillins, penicillins combined with beta-lactamase, cephalosporins, and metronidazole penetrate the pleural space well. Aminoglycosides should be avoided due to their poor penetration of the pleural space and decreased efficacy in acidic environments. Clindamycin can be used as an alternative to metronidazole.
- Intrapleural administration of antibiotics is not recommended.
- If possible, antibiotic choice should be based on bacterial culture from the pleural fluid.
- Even when anaerobic cultures are negative, continuation of empirical antibiotics covering both common community-acquired bacterial pathogens and anaerobic organisms should be considered, because anaerobes frequently infect empyemas and because anaerobes are not always cultured successfully.
- In general, empirical antibiotics with activity against atypical organisms are not necessary.
- For patients with community-acquired empyemas in whom the risk for methicillin-resistant *Staphylococcus aureus* and highly resistant gram-negative infection is low, the recommended treatment is with a second- or third-generation cephalosporin (e.g., cefuroxime, ceftriaxone) or an aminopenicillin with a beta-lactamase inhibitor (e.g., ampicillin/sulbactam). However, due to emergent resistance patterns clinicians should familiarize themselves with a local antibiogram. Ampicillin/sulbactam is active against a range of anaerobes, but ceftriaxone requires the addition of an antibiotic with anaerobic cover, such as metronidazole. Clindamycin may be used as an alternative to metronidazole.
- Empirical antibiotic treatment for hospital-acquired empyema should include antibiotics active against methicillin-resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa* (e.g.,

vancomycin plus cefepime, and metronidazole; or vancomycin plus piperacillin/tazobactam) and keep in mind increasing resistance patterns. Vancomycin plus meropenem may be indicated if there is a history or suspicion of extended spectrum beta-lactamase-producing organisms. As up to 25% of cases of hospital-acquired empyema are associated with MRSA, all patients (particularly postoperative and post-traumatic) should receive anti-staphylococcal cover.

#### Subsequent antibiotic therapy[8]

- Once culture results from the pleural fluid are obtained, antibiotics should be tailored to the sensitivities of the grown culture. Antibiotics should not be discontinued following a negative culture, as pleural fluid cultures are negative in 40% of cases. In these patients, prolonged empirical antibiotic therapy may be required.
- If the patient has responded to intravenous treatment, the source of infection has been controlled, the organism is susceptible to oral antibiotics, and the patient's oral intake is acceptable, then a transition to oral treatment can be made.
- Although the optimum duration of treatment is unknown, antibiotic therapy is generally continued for at least 3 weeks. The Working Group of the American Association for Thoracic Surgery recommends a minimum of 2 weeks from the time of drainage and settling of the fever, and states that clinical response, source control, and pathogen should all play a role in treatment decisions. Inflammatory markers (white blood cell count [WBC] and C-reactive protein [CRP]) are useful as guides to the required duration of antibiotic treatment.
- Prolonged courses of antibiotics may be necessary and can be administered after discharge.

#### Supportive care

- Antipyretics and analgesics should be administered as indicated. The authors make no recommendations for specific antipyretics and analgesics. Agents should be used in accordance with local protocols. Good nursing care, ensuring maintenance of appropriate dietary intake with nutritional supplements if necessary, is paramount. Early mobilization is also essential.

#### Chest tube drainage

- Urgent chest drain insertion is essential in all adults with empyema or complicated parapneumonic effusion. In most cases thoracentesis alone is not sufficient.
- Chest drains should be inserted by competent personnel under imaging (ultrasound) guidance to reduce the risk of complications that include organ damage, hemorrhage, subcutaneous emphysema, and death.[40]
- There is no consensus on the optimal chest tube size for drainage, although it is likely that small-bore chest drains (10-14F) are as effective as large-bore drains (20-28F).[8] [41] Small-bore drains have also been shown to be less painful for patients.[42]
- Regular flushing with saline is recommended for small-bore chest drains and if the chest drain becomes blocked.
- The chest drain should remain in place until the effusion has resolved and drainage has stopped.

#### Surgery

- Patients who do not respond to antibiotics and tube thoracostomy (chest drain insertion) should be referred to a thoracic surgeon for consideration of surgical intervention. Failure to respond is a



clinical decision based on ongoing fever, failure of pleural fluid drainage, and persistently raised inflammatory markers. Approximately 30% of patients will require surgery.[23]

- The optimal time at which to refer for surgery is unclear. Some authorities advocate immediate surgery for all patients. The American Association for Thoracic Surgery recommends VATS as the first-line approach in all patients with stage 2 acute empyema.[8] However, some experts support a trial of combination therapy with a fibrinolytic drug and dornase alfa before considering surgery for patients with stage 2 empyema, or for patients with stage 3 empyema awaiting a surgical consultation.[43] In patients with stage 2 and 3 empyema, a beneficial effect of surgical debridement or decortication has been found over tube thoracostomy alone in terms of treatment success and reduction in hospital stay. For patients with stage 3 empyema VATS has been shown in some studies to be as effective as open decortication. However, there were some series reporting high conversion rate to open decortication (about 40%). Stage 3 empyema decortication should be performed by open technique, particularly in symptomatic patients over 5 weeks; in experienced units VATS may be an option, especially in early surgical referrals.[22]
- The first-line surgical option is VATS, as it is a less invasive procedure, with less postoperative pain, shorter hospital length of stay, less blood loss, less respiratory compromise, fewer postoperative complications, and lower cost compared with open thoracotomy.[8]
- Local anesthetic thoracoscopy may be useful for the treatment of empyema, allowing division of septations and adhesions and facilitating accurate tube placement and drainage, but is not routinely used, as large prospective randomized trials are still needed to elucidate its role for empyema.
- A thoracic surgeon should be involved in assessment of the patient, even for anesthesia. Less radical surgical interventions, depending on surgical expertise and access, such as rib resection and placement of a large-bore drain, may be considered in unstable patients and can be performed in some cases with epidural or local anesthesia.[8]
- In patients with ineffective effusion drainage and persistent sepsis who cannot tolerate general anesthesia, re-evaluation with re-imaging of the thorax and, after discussion with a thoracic surgeon, placement of another image-guided small-bore catheter or a larger bore chest tube, or intrapleural enzyme therapy may be considered.[8]
- If VATS is not available, intrapleural enzyme therapies should be considered, and if these do not result in adequate resolution of the empyema, further surgical options should be discussed with a thoracic surgeon. These include mini-thoracotomy, decortication (a major thoracic operation involving the evacuation of pus and debris from the pleural space and removal of fibrous tissue from the visceral and parietal pleura), and open thoracic drainage. Intrapleural fibrinolytic drugs should be considered for patients who are not surgical candidates.

#### Intrapleural enzyme therapy

- As of November 2023 there has not been a head to head randomized controlled trial comparing early surgery to chest tube thoracostomy with intrapleural enzyme therapy. However, it is likely that early intervention in general has significant benefit and is associated with shorter hospital length of stay.[37]
- Standard medical therapy with chest tube thoracostomy and antibiotics fail in approximately 30% of adult patients. These patients should be treated with either surgical intervention, or intrapleural enzyme therapy with a combination of alteplase (recombinant tissue plasminogen activator [t-PA]) and dornase alfa (deoxyribonuclease [DNase]). The medications are instilled into the chest tube and allowed to dwell for 1 hour.

- Intrapleural enzyme therapy may be indicated for the decompression of multiloculated and tube drainage-resistant pleural effusions that are responsible for dyspnea or respiratory failure if a thoracic surgeon identifies that surgery is not immediately possible (e.g., patient comorbidity or other clinical or logistical reasons).[44] Some experts support routine consideration of intrapleural enzyme therapy for either initial or subsequent treatment of empyema, but only following multidisciplinary risk-benefit discussion and depending on local expertise and the availability of minimally invasive surgical services.[43]
- Intrapleural enzyme therapy (such as streptokinase or urokinase) should be considered in hemodynamically unstable and older patients, patients who are not candidates for surgery (e.g., due to comorbidity), in those with a large effusion not relieved by chest tube drainage and causing respiratory compromise, and in institutions where VATS is not available.[45] [46] American Association for Thoracic Surgery guidelines do not support routine use of intrapleural fibrinolytics for complicated pleural effusions and early empyemas.[8]
- The bleeding risk from intrapleural enzyme therapy is low. In one large multicenter retrospective review of 1833 patients, there was a 4.1% bleeding risk associated with intrapleural enzyme therapy. Increased risk of bleeding was associated with therapeutic anticoagulation, increased RAPID [Renal (urea), Age, fluid Purulence, Infection source, Dietary (albumin)] score, increased serum urea, and thrombocytopenia ( $<100 \times 10^9/L$ ).[47]
- Most experts recommend use of a combination of a fibrinolytic and dornase alfa in place of monotherapy.[43]

#### Indwelling pleural catheters

- These may rarely have a role in maintaining drainage of a chronically infected pleural space that is not readily treated in other ways such as surgery.[48]
- Patients with existing indwelling pleural catheters placed for malignant pleural effusion who develop pleural space infections can often be treated with antibiotics and pleural fluid drainage without removal of the indwelling pleural catheter.[49] The catheter should likely be removed if patients present with sepsis.

## Children

#### Antibiotic therapy

- All children with empyema should be treated with empirical intravenous antibiotics covering *Streptococcus pneumoniae* and *Staphylococcus aureus*, based on local microbiology guidelines.[26] [27] Antibiotics should be administered intravenously in high doses initially to ensure adequate pleural penetration.[27] Once culture results from the pleural fluid are obtained, antibiotics may be tailored to the sensitivities of the grown culture. Antibiotics should not be discontinued following a negative culture, as pleural fluid cultures are negative in 40% of cases. In these patients, prolonged empirical antibiotic therapy may be required.[50]
- Antibiotic selection for empyemas varies and selection should be based on local microbiology guidelines; however, suitable choices include cefotaxime or ceftriaxone or ampicillin, depending on local guidelines or antibiograms.[26] The addition of vancomycin or linezolid is usually reserved for culture-proven or severe suspected MRSA infection.[26]

- When drainage has been completed, and the patient is clinically improving and off oxygen, the route of antibiotic administration may be changed to oral.[26] Inflammatory markers (WBC count and CRP) are useful as guides to the required duration of antibiotic treatment.

#### Supportive care

- Supplemental oxygen should be provided to children with  $\text{SaO}_2 < 93\%$ . [27] Antipyretics and analgesics should be administered as indicated. The authors make no recommendations for specific antipyretics and analgesics. Good nursing care, ensuring maintenance of appropriate dietary intake with nutritional supplements if necessary, is paramount. Early mobilization is also essential.

#### Chest tube drainage

- Urgent chest drain insertion is essential in all children with empyema or complicated parapneumonic effusion.[8] [50]
- Chest drains should be inserted by competent personnel under ultrasound guidance to reduce the risk of complications that include organ damage, hemorrhage, subcutaneous emphysema, and death.[40]
- Small drains should be used whenever possible to minimize patient discomfort.
- The chest drain should remain in place until the effusion has resolved and drainage has stopped.

#### Intrapleural enzyme therapy

- If antibiotics and chest tube drainage do not result in adequate resolution of the empyema, intrapleural enzyme therapy should be considered.[18]
- Most experts recommend use of a combination of a fibrinolytic and DNase in place of monotherapy.[43]
- Urokinase is the only fibrinolytic drug that has been studied and recommended for use in children, but it has not been available in the US for many years.[51] [52] Alteplase is a suitable alternative option.[26] [27] Although it has been successfully evaluated in pediatric patients with empyema, some data show no difference in length of hospital stay between chest tube drainage and use of intrapleural alteplase.[53]

#### Surgery

- Children who do not respond to antibiotics and tube thoracostomy (chest drain insertion) should be referred to a thoracic surgeon for consideration of VATS.[27] [48] Failure to respond is a clinical judgment based on ongoing fever, failure of pleural fluid drainage, and persistently raised inflammatory markers.[8]
- Management of empyema in children with VATS is a safe and effective method, but nonsurgical management with tube thoracostomy and fibrinolytics has been shown to be equally successful. Children with empyema should be managed with either treatment, based on local expertise and success rates.[26]
- If VATS is not available or does not result in adequate resolution of the empyema, further surgical options should be discussed with a thoracic surgeon. VATS debridement is preferred over open thoracotomy.[8] Mini-thoracotomy is the first choice of other surgical procedures. Organized empyemas in symptomatic children may require open surgery or decortication, a major thoracic operation involving the evacuation of pus and debris from the pleural space and removal of fibrous tissue from the visceral and parietal pleura.[50]

# Treatment algorithm overview

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: [see disclaimer](#)

Initial		( summary )	
adults (culture results pending)			
■ with community-acquired empyema	1st	empirical intravenous antibiotics	
	plus	chest tube drainage	
	plus	supportive care	
	adjunct	fluid resuscitation	
■ with hospital-acquired empyema	1st	empirical intravenous antibiotics	
	plus	chest tube drainage	
	plus	supportive care	
	adjunct	fluid resuscitation	
children (culture results pending)			
	1st	empirical intravenous antibiotics	
	plus	chest tube drainage	
	plus	supportive care	
	adjunct	fluid resuscitation	

<b>Acute ( summary )</b>		
<b>adults (culture results available)</b>		
	<b>1st</b>	<b>antibiotics according to culture sensitivity</b>
	<b>plus</b>	<b>chest tube drainage</b>
	<b>plus</b>	<b>supportive care</b>
	<b>adjunct</b>	<b>intrapleural enzyme therapy</b>
	<b>2nd</b>	<b>video-assisted thoracoscopic surgery (VATS)</b>
	<b>plus</b>	<b>supportive care + continued antibiotics</b>
	<b>3rd</b>	<b>intrapleural enzyme therapy</b>
	<b>plus</b>	<b>supportive care + continued antibiotics</b>
	<b>4th</b>	<b>mini-thoracotomy, decortication, or open thoracic drainage</b>
	<b>plus</b>	<b>supportive care + continued antibiotics</b>
	<b>5th</b>	<b>indwelling pleural catheter</b>
	<b>plus</b>	<b>supportive care + continued antibiotics</b>
<b>children (culture results available)</b>		
	<b>1st</b>	<b>antibiotics according to culture sensitivity</b>
	<b>plus</b>	<b>chest tube drainage</b>
	<b>plus</b>	<b>supportive care</b>
	<b>2nd</b>	<b>intrapleural enzyme therapy</b>
	<b>plus</b>	<b>supportive care + continued antibiotics</b>
	<b>3rd</b>	<b>video-assisted thoracoscopic surgery (VATS)</b>
	<b>plus</b>	<b>supportive care + continued antibiotics</b>
	<b>4th</b>	<b>mini-thoracotomy, decortication, or open thoracic drainage</b>
	<b>plus</b>	<b>supportive care + continued antibiotics</b>

# Treatment algorithm

Please note that formulations/routes and doses may differ between drug names and brands, drug formularies, or locations. Treatment recommendations are specific to patient groups: [see disclaimer](#)

## Initial

### adults (culture results pending)

- with community-acquired empyema

1st

#### empirical intravenous antibiotics

##### Primary options

- » [cefuroxime sodium](#): 750-1500 mg intravenously every 6-8 hours
- or-
- » [ceftriaxone](#): 1-2 g intravenously every 12-24 hours

##### --AND--

- » [metronidazole](#): 15 mg/kg intravenously as a loading dose, followed by 7.5 mg/kg every 6 hours, maximum 4000 mg/day
- or-
- » [clindamycin](#): 600 mg intravenously every 6-12 hours; or 900 mg intravenously every 8-12 hours

OR

- » [ampicillin/sulbactam](#): 1-2 g intravenously every 6 hours
- Dose refers to ampicillin component.

» All adults should initially receive empirical intravenous antibiotics based on local microbiology guidelines to cover the likely causative organisms, both aerobic and anaerobic. Clinicians should keep in mind differences between community-acquired and hospital-acquired pathogens. Once culture results from the pleural fluid are obtained, antibiotics may be tailored to the sensitivities of the grown culture.<sup>[8]</sup>

» For patients with community-acquired empyemas in whom the risk for methicillin-resistant *Staphylococcus aureus* and highly resistant gram-negative infection is low, the recommended treatment is with a second- or third-generation cephalosporin (e.g., cefuroxime, ceftriaxone) or an aminopenicillin with a beta-lactamase inhibitor (e.g., ampicillin/sulbactam). However, due to emergent resistance patterns, clinicians should familiarize themselves with a local antibiogram. Ampicillin/sulbactam is active against a range of anaerobes, but ceftriaxone requires the addition of an antibiotic



# Initial

with anaerobic cover, such as metronidazole. Clindamycin may be used as an alternative to metronidazole.[8]

» In general, empirical antibiotics with activity against atypical organisms are not necessary.[8]

## plus chest tube drainage

Treatment recommended for ALL patients in selected patient group

» Urgent chest drain insertion is essential in all adults with empyema or complicated parapneumonic effusion.[8]

» Chest drains should be inserted by competent personnel under imaging (ultrasound) guidance to reduce the risk of complications that include organ damage, hemorrhage, subcutaneous emphysema, and death.[8] [40]

» There is no consensus on the optimal chest tube size for drainage, although it is likely that small-bore chest drains (10-14F) are as effective as large-bore drains (20-28F).[8] [41] Small-bore drains have also been shown to be less painful for patients.[42] Regular flushing with saline is recommended for small-bore chest drains and if the chest drain becomes blocked.[8]

» The chest drain should remain in place until the effusion has resolved and drainage has stopped.

## plus supportive care

Treatment recommended for ALL patients in selected patient group

» Antipyretics and analgesics should be administered as indicated. The authors make no recommendations for specific antipyretics and analgesics. Agents should be used in accordance with local protocols.

» Good nursing care, ensuring maintenance of appropriate dietary intake with nutritional supplements if necessary, is paramount. Early mobilization is also essential.

## adjunct fluid resuscitation

Treatment recommended for SOME patients in selected patient group

» Patients may be septic at presentation and require emergency fluid resuscitation and urgent intravenous antibiotics even before the diagnosis is established.

## Initial

■ with hospital-acquired empyema

1st

empirical intravenous antibiotics

Primary options

» **vancomycin**: 500 mg intravenously every 6 hours; or 1000 mg intravenously every 12 hours

--AND--

» **cefepime**: 2 g intravenously every 8 hours

--AND--

» **metronidazole**: 15 mg/kg intravenously as a loading dose, followed by 7.5 mg/kg every 6 hours, maximum 4000 mg/day

-or-

» **clindamycin**: 600 mg intravenously every 6-12 hours; or 900 mg intravenously every 8-12 hours

OR

» **vancomycin**: 500 mg intravenously every 6 hours; or 1000 mg intravenously every 12 hours

-and-

» **piperacillin/tazobactam**: 4.5 g intravenously every 6 hours

Dose refers to 4 g piperacillin plus 0.5 g tazobactam.

OR

» **vancomycin**: 500 mg intravenously every 6 hours; or 1000 mg intravenously every 12 hours

-and-

» **meropenem**: 1 g intravenously every 8 hours

» All adults should initially receive empirical intravenous antibiotics based on local microbiology guidelines to cover the likely causative organisms, both aerobic and anaerobic. Clinicians should keep in mind differences between community-acquired and hospital-acquired pathogens. Once culture results from the pleural fluid are obtained, antibiotics may be tailored to the sensitivities of the grown culture.<sup>[8]</sup>

» Empirical antibiotic treatment for hospital-acquired empyema should include antibiotics active against methicillin-resistant *Staphylococcus aureus* and *Pseudomonas aeruginosa* (e.g., vancomycin plus cefepime, and metronidazole; or vancomycin plus

## Initial

piperacillin/tazobactam) and keep in mind increasing resistance patterns. Clindamycin may be used as an alternative to metronidazole. Vancomycin plus meropenem may be indicated if there is a history or suspicion of extended spectrum beta-lactamase-producing organisms.[8] As up to 25% of cases of hospital-acquired empyema are associated with MRSA, all patients (particularly postoperative and post-traumatic) should receive anti-staphylococcal cover.[8]

» In general, empirical antibiotics with activity against atypical organisms are not necessary.[8]

»

### plus chest tube drainage

Treatment recommended for ALL patients in selected patient group

» Urgent chest drain insertion is essential in all adults with empyema or complicated parapneumonic effusion.[8]

» Chest drains should be inserted by competent personnel under imaging (ultrasound) guidance to reduce the risk of complications that include organ damage, hemorrhage, subcutaneous emphysema, and death.[8] [40]

» There is no consensus on the optimal chest tube size for drainage, although it is likely that small-bore chest drains (10-14F) are as effective as large-bore drains (20-28F).[8] [41] Small-bore drains have also been shown to be less painful for patients.[42] Regular flushing with saline is recommended for small-bore chest drains and if the chest drain becomes blocked.[8]

» The chest drain should remain in place until the effusion has resolved and drainage has stopped.

### plus supportive care

Treatment recommended for ALL patients in selected patient group

» Antipyretics and analgesics should be administered as indicated. The authors make no recommendations for specific antipyretics and analgesics. Agents should be used in accordance with local protocols.

» Good nursing care, ensuring maintenance of appropriate dietary intake with nutritional supplements if necessary, is paramount. Early mobilization is also essential.

# Initial

## adjunct fluid resuscitation

Treatment recommended for SOME patients in selected patient group

» Patients may be septic at presentation and require emergency fluid resuscitation and urgent intravenous antibiotics even before the diagnosis is established.

## children (culture results pending)

## 1st empirical intravenous antibiotics

### Primary options

» **cefotaxime**: body weight <50 kg: 150-180 mg/kg/day intravenously given in divided doses every 8 hours, maximum 8 g/day; body weight ≥50 kg: 1-2 g intravenously every 6-8 hours

### OR

» **ceftriaxone**: 50-100 mg/kg/day intravenously given in divided doses every 12-24 hours, maximum 4 g/day

### OR

» **ampicillin**: 150-400 mg/kg/day intravenously given in divided doses every 6 hours, maximum 12 g/day

### OR

» **cefotaxime**: body weight <50 kg: 150-180 mg/kg/day intravenously given in divided doses every 8 hours, maximum 8 g/day; body weight ≥50 kg: 1-2 g intravenously every 6-8 hours

### -or-

» **ceftriaxone**: 50-100 mg/kg/day intravenously given in divided doses every 12-24 hours, maximum 4 g/day

### -or-

» **ampicillin**: 150-400 mg/kg/day intravenously given in divided doses every 6 hours, maximum 12 g/day

### --AND--

» **vancomycin**: 60 mg/kg/day intravenously given in divided doses every 6 hours

### -or-

» **linezolid**: children <12 years of age: 10 mg/kg (maximum 600 mg/dose) intravenously every 8 hours; children ≥12 years of age: 600 mg intravenously every 12 hours

## Initial

» All children should initially receive empirical intravenous antibiotics based on local microbiology guidelines to cover the likely causative organisms.[26]

» Antibiotics covering *Streptococcus pneumoniae* and *Staphylococcus aureus* [26] [27] should be given.

» Suitable choices include cefotaxime or ceftriaxone or ampicillin, depending on local guidelines or antibiograms.[26] The addition of vancomycin or linezolid is usually reserved for culture-proven or severe suspected MRSA infection.[26]

» Once culture results from the pleural fluid are obtained, antibiotics may be tailored to the sensitivities of the grown culture.

**plus chest tube drainage**

Treatment recommended for ALL patients in selected patient group

» Urgent chest drain insertion is essential in all children with empyema or complicated parapneumonic effusion.[8] [50]

» Chest drains should be inserted by competent personnel under imaging (ultrasound) guidance to reduce the risk of complications that include organ damage, hemorrhage, subcutaneous emphysema, and death.[40]

» Small drains should be used whenever possible to minimize patient discomfort.

» The chest drain should remain in place until the effusion has resolved and drainage has stopped.

**plus supportive care**

Treatment recommended for ALL patients in selected patient group

» Supplemental oxygen should be provided to children with SaO<sub>2</sub> <93%.[27]

» Antipyretics and analgesics should be administered as indicated. The authors make no recommendations for specific antipyretics and analgesics. Agents should be used in accordance with local protocols.

» Good nursing care, ensuring maintenance of appropriate dietary intake with nutritional supplements if necessary, is paramount. Early mobilization is also essential.

**Initial****adjunct    fluid resuscitation**

Treatment recommended for SOME patients in selected patient group

» Patients may be septic at presentation and require emergency fluid resuscitation and urgent intravenous antibiotics even before the diagnosis is established.

# Acute

adults (culture results available)

1st

## antibiotics according to culture sensitivity

» Once culture results from the pleural fluid are obtained, antibiotics should be tailored to the sensitivities of the grown culture.[8]

» Antibiotics should not be discontinued following a negative culture, as pleural fluid cultures are negative in 40% of cases. In these patients, prolonged empirical antibiotic therapy may be required.[50] Even when anaerobic cultures are negative, continuation of empirical antibiotics covering both common community-acquired bacterial pathogens and anaerobic organisms should be considered, because anaerobes frequently infect empyemas and because anaerobes are not always cultured successfully.[8]

» If the patient has responded to intravenous treatment, the source of infection has been controlled, the organism is susceptible to oral antibiotics, and the patient's oral intake is acceptable, then a transition to oral treatment can be made.[8]

» Although the optimum duration of treatment is unknown, antibiotic therapy is generally continued for at least 3 weeks. The Working Group of the American Association for Thoracic Surgery recommends a minimum of 2 weeks from the time of drainage and settling of the fever, and states that clinical response, source control, and pathogen should all play a role in treatment decisions.[8]

» Inflammatory markers (WBC count and CRP) are useful as guides to the required duration of antibiotic treatment.

plus

## chest tube drainage

Treatment recommended for ALL patients in selected patient group

» Urgent chest drain insertion is essential in all adults with empyema or complicated parapneumonic effusion.[8]

» Chest drains should be inserted by competent personnel under imaging (ultrasound) guidance to reduce the risk of complications that include organ damage, hemorrhage, subcutaneous emphysema, and death.[8] [40]



## Acute

» There is no consensus on the optimal chest tube size for drainage, although it is likely that small-bore chest drains (10-14F) are as effective as large-bore drains (20-28F).<sup>[8]</sup> <sup>[41]</sup> Small-bore drains have also been shown to be less painful for patients.<sup>[42]</sup>

» Regular flushing with saline is recommended for small-bore chest drains and if the chest drain becomes blocked.<sup>[8]</sup>

» The chest drain should remain in place until the effusion has resolved and drainage has stopped.

**plus****supportive care**

Treatment recommended for ALL patients in selected patient group

» Intravenous fluid treatment for sepsis should be continued as required.

» Antipyretics and analgesics should be administered as indicated. The authors make no recommendations for specific antipyretics and analgesics. Agents should be used in accordance with local protocols.

» Good nursing care, ensuring maintenance of appropriate dietary intake with nutritional supplements if necessary, is paramount. Early mobilization is also essential.

**adjunct****intrapleural enzyme therapy**

Treatment recommended for SOME patients in selected patient group

**Primary options**

» **alteplase**: 10 mg intrapleurally twice daily for 3 days

**-and-**

» **dornase alfa inhaled**: 5 mg intrapleurally twice daily for 3 days

» Intrapleural enzyme therapy consists of a combination of alteplase (recombinant tissue plasminogen activator [t-PA]) and dornase alfa (deoxyribonuclease [DNase]). The medications are instilled into the chest tube and allowed to dwell for 1 hour.

» Should be considered in hemodynamically unstable and older patients, patients who are not candidates for surgery (e.g., due to comorbidity), in those with a large effusion not relieved with chest tube drainage and causing respiratory compromise, and in institutions where video-assisted thoracoscopic surgery

## Acute

is not available.[45] [46] American Association for Thoracic Surgery guidelines do not support routine use of intrapleural fibrinolytics for complicated pleural effusions and early empyemas.[8]

» Some experts support routine consideration of intrapleural enzyme therapy for either initial or subsequent treatment of empyema, but only following multidisciplinary risk-benefit discussion and depending on local expertise and the availability of minimally invasive surgical services.[43]

» Most experts support use of a combination of a fibrinolytic and dornase alfa in place of monotherapy.[43]

## 2nd video-assisted thoracoscopic surgery (VATS)

» Patients who do not respond to antibiotics and tube thoracostomy (chest drain insertion) should be referred to a thoracic surgeon for consideration of surgical intervention. Failure to respond is a clinical decision based on ongoing fever, failure of pleural fluid drainage, and persistently raised inflammatory markers. Approximately 30% of patients will require surgery.[23] However, some experts support a trial of combination therapy with a fibrinolytic agent and dornase alfa before considering surgery for patients with stage 2 empyema, or for patients with stage 3 empyema awaiting a surgical consultation.[43]

» The optimal time at which to refer for surgery is unclear. Some authorities advocate immediate surgery for all patients, but this is debated. The American Association for Thoracic Surgery recommends VATS as the first-line approach in all patients with stage 2 acute empyema.[8]

» The first-line surgical option is VATS, as it is a less invasive procedure, with less postoperative pain, shorter hospital length of stay, less blood loss, less respiratory compromise, fewer postoperative complications, and lower cost compared with open thoracotomy.[8]

» In patients with ineffective effusion drainage and persistent sepsis who cannot tolerate general anesthesia, re-evaluation with re-imaging of the thorax and, after discussion with a thoracic surgeon, placement of another image-guided small-bore catheter or a larger bore chest tube, or intrapleural fibrinolytic may be considered.[8]

## Acute

**plus supportive care + continued antibiotics**

Treatment recommended for ALL patients in selected patient group

» Intravenous fluid treatment for sepsis should be continued as required.

» Antipyretics and analgesics should be administered as indicated. The authors make no recommendations for specific antipyretics and analgesics. Agents should be used in accordance with local protocols.

» Good nursing care, ensuring maintenance of appropriate dietary intake with nutritional supplements if necessary, is paramount. Early mobilization is also essential.

» Antibiotics should be continued. If the patient has responded to intravenous treatment, the source of infection has been controlled, the organism is susceptible to oral antibiotics, and the patient's oral intake is acceptable, then a transition to oral treatment can be made.[8]

» Although the optimum duration of treatment is unknown, antibiotic therapy is generally continued for at least 3 weeks. The Working Group of the American Association for Thoracic Surgery recommends a minimum of 2 weeks from the time of drainage and settling of the fever, and states that clinical response, source control, and pathogen should all play a role in treatment decisions.[8] Inflammatory markers (WBC count and CRP) are useful as guides to the required duration of antibiotic treatment.

**3rd intrapleural enzyme therapy****Primary options**

» **alteplase**: 10 mg intrapleurally twice daily for 3 days

**-and-**

» **dornase alfa inhaled**: 5 mg intrapleurally twice daily for 3 days

» Intrapleural enzyme therapy consists of a combination of alteplase (recombinant tissue plasminogen activator [t-PA]) and dornase alfa (deoxyribonuclease [(DNase)]). The medications are instilled into the chest tube and allowed to dwell for 1 hour.

» May be indicated for the decompression of multiloculated and tube drainage-resistant pleural effusions that are responsible for dyspnea or respiratory failure if a thoracic

## Acute

surgeon identifies that surgery is not immediately possible (e.g., patient comorbidity or other clinical or logistical reasons).[44] Some experts support routine consideration of intrapleural enzyme therapy for either initial or subsequent treatment of empyema, but only following multidisciplinary risk-benefit discussion and depending on local expertise and the availability of minimally invasive surgical services.[43]

» Intrapleural enzyme therapy should be considered in hemodynamically unstable and older patients, patients who are not candidates for surgery (e.g., due to comorbidity), in those with a large effusion not relieved with chest tube drainage and causing respiratory compromise, and in institutions where VATS is not available.[45] [46] American Association for Thoracic Surgery guidelines do not support routine use of intrapleural fibrinolytics for complicated pleural effusions and early empyemas.[8]

» Most experts recommend use of a combination of a fibrinolytic and dornase alfa in place of monotherapy.[43]

**plus****supportive care + continued antibiotics**

Treatment recommended for ALL patients in selected patient group

» Intravenous fluid treatment for sepsis should be continued as required.

» Antipyretics and analgesics should be administered as indicated. The authors make no recommendations for specific antipyretics and analgesics. Agents should be used in accordance with local protocols.

» Good nursing care, ensuring maintenance of appropriate dietary intake with nutritional supplements if necessary, is paramount. Early mobilization is also essential.

» Antibiotics should be continued. If the patient has responded to intravenous treatment, the source of infection has been controlled, the organism is susceptible to oral antibiotics, and the patient's oral intake is acceptable, then a transition to oral treatment can be made.[8]

» Although the optimum duration of treatment is unknown, antibiotic therapy is generally continued for at least 3 weeks. The Working Group of the American Association for Thoracic Surgery recommends a minimum of 2 weeks from the time of drainage and settling of the

## Acute

fever, and states that clinical response, source control, and pathogen should all play a role in treatment decisions.[8] Inflammatory markers (WBC count and CRP) are useful as guides to the required duration of antibiotic treatment.

#### 4th **mini-thoracotomy, decortication, or open thoracic drainage**

» If there is inadequate resolution of the empyema following video-assisted thoracoscopic surgery or intrapleural enzyme therapy, further surgical options should be discussed with a thoracic surgeon.

» These include mini-thoracotomy, decortication (a major thoracic operation involving the evacuation of pus and debris from the pleural space and removal of fibrous tissue from the visceral and parietal pleura), and open thoracic drainage.

» Local anesthetic thoracoscopy may be useful for the treatment of empyema, allowing division of septations and adhesions and facilitating accurate tube placement and drainage, but is not routinely used, as large prospective randomized trials are still needed to elucidate its role for empyema.

» A thoracic surgeon should be involved in assessment of the patient, even for anesthesia. Less radical surgical interventions, depending on surgical expertise and access, such as rib resection and placement of a large-bore drain, may be considered in unstable patients and can be performed in some cases with epidural or local anesthesia.

#### **plus supportive care + continued antibiotics**

Treatment recommended for ALL patients in selected patient group

» Intravenous fluid treatment for sepsis should be continued as required.

» Antipyretics and analgesics should be administered as indicated. The authors make no recommendations for specific antipyretics and analgesics. Agents should be used in accordance with local protocols.

» Good nursing care, ensuring maintenance of appropriate dietary intake with nutritional supplements if necessary, is paramount. Early mobilization is also essential.

» Antibiotics should be continued. If the patient has responded to intravenous treatment, the

## Acute

source of infection has been controlled, the organism is susceptible to oral antibiotics, and the patient's oral intake is acceptable, then a transition to oral treatment can be made.[8]

» Although the optimum duration of treatment is unknown, antibiotic therapy is generally continued for at least 3 weeks. The Working Group of the American Association for Thoracic Surgery recommends a minimum of 2 weeks from the time of drainage and settling of the fever, and states that clinical response, source control, and pathogen should all play a role in treatment decisions.[8] Inflammatory markers (WBC count and CRP) are useful as guides to the required duration of antibiotic treatment.

### 5th indwelling pleural catheter

» May rarely have a role in maintaining drainage of a chronically infected pleural space that is not readily treated in other ways such as surgery.

### plus supportive care + continued antibiotics

Treatment recommended for ALL patients in selected patient group

» Intravenous fluid treatment for sepsis should be continued as required.

» Antipyretics and analgesics should be administered as indicated. The authors make no recommendations for specific antipyretics and analgesics. Agents should be used in accordance with local protocols.

» Good nursing care, ensuring maintenance of appropriate dietary intake with nutritional supplements if necessary, is paramount. Early mobilization is also essential.

» Antibiotics should be continued. If the patient has responded to intravenous treatment, the source of infection has been controlled, the organism is susceptible to oral antibiotics, and the patient's oral intake is acceptable, then a transition to oral treatment can be made.[8]

» Although the optimum duration of treatment is unknown, antibiotic therapy is generally continued for at least 3 weeks. The Working Group of the American Association for Thoracic Surgery recommends a minimum of 2 weeks from the time of drainage and settling of the fever, and states that clinical response, source control, and pathogen should all play a role in treatment decisions.[8] Inflammatory markers (WBC count and CRP) are useful as guides to the required duration of antibiotic treatment.

## Acute

children (culture results available)

- 1st antibiotics according to culture sensitivity**
- » Once culture results from the pleural fluid are obtained, antibiotics may be tailored to the sensitivities of the grown culture.
  - » Antibiotics should not be discontinued following a negative culture as pleural fluid cultures are negative in 40% of cases. In these patients, prolonged empirical antibiotic therapy may be required.[\[50\]](#)
  - » When drainage has been completed, and the patient is clinically improving and off oxygen, the route of antibiotic administration may be changed to oral.[\[26\]](#)
  - » Inflammatory markers (WBC count and CRP) are useful as guides to the required duration of antibiotic treatment.
- plus chest tube drainage**
- Treatment recommended for ALL patients in selected patient group
- » Urgent chest drain insertion is essential in all children with empyema or complicated parapneumonic effusion.[\[8\]](#) [\[50\]](#)
  - » Chest drains should be inserted by competent personnel under imaging (ultrasound) guidance to reduce the risk of complications that include organ damage, hemorrhage, subcutaneous emphysema, and death.[\[40\]](#)
  - » Small drains should be used whenever possible to minimize patient discomfort.
  - » The chest drain should remain in place until the effusion has resolved and drainage has stopped.
- plus supportive care**
- Treatment recommended for ALL patients in selected patient group
- » Supplemental oxygen should be provided to children with  $\text{SaO}_2 < 93\%$ .[\[27\]](#)
  - » Intravenous fluid treatment for sepsis should be continued as required.
  - » Antipyretics and analgesics should be administered as indicated. The authors make no recommendations for specific antipyretics



# Acute

and analgesics. Agents should be used in accordance with local protocols.

» Good nursing care, ensuring maintenance of appropriate dietary intake with nutritional supplements if necessary, is paramount. Early mobilization is also essential.

## 2nd intrapleural enzyme therapy

### Primary options

» **alteplase**: 10 mg intrapleurally twice daily for 3 days

**-and-**

» **dornase alfa inhaled**: 5 mg intrapleurally twice daily for 3 days

» Most experts recommend use of a combination of a fibrinolytic and deoxyribonuclease (DNase) in place of monotherapy.[43] The medications are instilled into the chest tube and allowed to dwell for 1 hour.

» Should be considered if antibiotics and chest tube drainage do not result in adequate resolution of the empyema.

» Urokinase is the only fibrinolytic drug that has been studied and recommended in children, but it has not been available in the US for many years.[51] [52] Alteplase (recombinant tissue plasminogen activator) is a suitable alternative option.[26] [27] Although it has been successfully evaluated in pediatric patients with empyema, some data show no difference in length of hospital stay between chest tube drainage and use of intrapleural alteplase.[53]

## plus supportive care + continued antibiotics

Treatment recommended for ALL patients in selected patient group

» Supplemental oxygen should be provided to children with SaO<sub>2</sub> <93%.[27]

» Intravenous fluid treatment for sepsis should be continued as required.

» Antipyretics and analgesics should be administered as indicated. The authors make no recommendations for specific antipyretics and analgesics. Agents should be used in accordance with local protocols.

» Good nursing care, ensuring maintenance of appropriate dietary intake with nutritional supplements if necessary, is paramount. Early mobilization is also essential.

## Acute

- » Antibiotics should be continued. When drainage has been completed, and the patient is clinically improving and off oxygen, the route of antibiotic administration may be changed to oral.<sup>[26]</sup> Inflammatory markers (WBC count and CRP) are useful as guides to the required duration of antibiotic treatment.
- 3rd video-assisted thoracoscopic surgery (VATS)**
- » Children who do not respond to antibiotics and tube thoracostomy (chest drain insertion) should be referred to a thoracic surgeon for consideration of VATS.<sup>[27] [50]</sup>
- » Failure to respond is a clinical judgment based on ongoing fever, failure of pleural fluid drainage, and persistently raised inflammatory markers.<sup>[8]</sup>
- plus supportive care + continued antibiotics**
- Treatment recommended for ALL patients in selected patient group
- » Supplemental oxygen should be provided to children with  $\text{SaO}_2 < 93\%$ .<sup>[27]</sup>
- » Intravenous fluid treatment for sepsis should be continued as required.
- » Antipyretics and analgesics should be administered as indicated. The authors make no recommendations for specific antipyretics and analgesics. Agents should be used in accordance with local protocols.
- » Good nursing care, ensuring maintenance of appropriate dietary intake with nutritional supplements if necessary, is paramount. Early mobilization is also essential.
- » Antibiotics should be continued. When drainage has been completed, and the patient is clinically improving and off oxygen, the route of antibiotic administration may be changed to oral.<sup>[26]</sup> Inflammatory markers (WBC count and CRP) are useful as guides to the required duration of antibiotic treatment.
- 4th mini-thoracotomy, decortication, or open thoracic drainage**
- » If video-assisted thoracoscopic surgery (VATS) is not available or does not result in adequate resolution of the empyema, further surgical options should be discussed with a thoracic surgeon. VATS debridement is preferred over open thoracotomy.<sup>[8]</sup> Mini-thoracotomy is the first choice of other surgical procedures.

## Acute

plus

» Organized empyemas in symptomatic children may require open surgery or decortication, a major thoracic operation involving the evacuation of pus and debris from the pleural space and removal of fibrous tissue from the visceral and parietal pleura.<sup>[50]</sup>

### supportive care + continued antibiotics

Treatment recommended for ALL patients in selected patient group

» Supplemental oxygen should be provided to children with SaO<sub>2</sub> <93%.<sup>[27]</sup>

» Intravenous fluid treatment for sepsis should be continued as required.

» Antipyretics and analgesics should be administered as indicated. The authors make no recommendations for specific antipyretics and analgesics. Agents should be used in accordance with local protocols.

» Good nursing care, ensuring maintenance of appropriate dietary intake with nutritional supplements if necessary, is paramount. Early mobilization is also essential.

» Antibiotics should be continued. When drainage has been completed, and the patient is clinically improving and off oxygen, the route of antibiotic administration may be changed to oral.<sup>[26]</sup> Inflammatory markers (WBC count and CRP) are useful as guides to the required duration of antibiotic treatment.

## Secondary prevention

The risk of developing a chronic pleural infection or trapped lung is minimized through adequate antibiotic treatment and drainage of the pleural cavity.

## Patient discussions

Patients should ensure that they are compliant with the treatment for empyema and other comorbid conditions. They should also be advised to stop smoking if applicable and reduce their alcohol intake if this is excessive.<sup>[8]</sup>

# Monitoring

## Monitoring

The majority of patients will be discharged from the hospital on oral antibiotics. These patients should be followed up in 2 to 4 weeks. Measurement of the C-reactive protein and white blood cell counts can help to assess the response to antibiotics and the required length of treatment.

Some patients (e.g., those who are not surgical candidates, or have an empyema which cannot be easily drained or a trapped lung) may require indefinite antibiotic treatment for chronic pleural infection.

A repeat chest x-ray (CXR) should be taken 4 to 6 weeks after discharge. Although invariably abnormal at discharge, most CXR changes resolve within 3 to 6 months with some residual pleural thickening.

Some patients develop restrictive pulmonary function as a result of residual pleural thickening following chest tube removal. This pleural thickening resolves in most patients within several months and the pulmonary function is usually near normal after 3 to 6 months. If reduced pulmonary function persists after 6 months and the patient is symptomatic, surgical decortication should be considered.

In children with *Staphylococcus aureus* or *Pseudomonas aeruginosa* empyema, an underlying cause such as immunodeficiency or cystic fibrosis should be considered.

All patients should be followed up until they have fully recovered.

## Complications

Complications	Timeframe	Likelihood
<b>septic shock</b>	<b>short term</b>	<b>high</b>
<p>Undertreated infection can lead to the development of septic shock.</p> <p>Key signs are tachycardia and hypotension (BP &lt;90/60) with associated pyrexia.</p> <p>This complication is preventable with early administration of antibiotics, fluid resuscitation, and chest drain insertion.</p> <p>Patients presenting with an empyema should have their vital signs monitored frequently for the early detection of septic shock.</p>		
<b>complications of chest drain insertion</b>	<b>short term</b>	<b>low</b>
<p>Recognized complications of chest drain insertion include organ damage, hemorrhage, subcutaneous emphysema, and death.<sup>[40]</sup></p> <p>Chest drains should be inserted by competent personnel under ultrasound guidance to reduce the risk of such complications.</p>		
<b>allergic reaction to intrapleural streptokinase</b>	<b>short term</b>	<b>low</b>
<p>This complication occurs uncommonly following intrapleural administration of streptokinase.</p> <p>Patients should receive an exposure card and alternative fibrinolytics in the future if these are ever indicated.</p> <p>Streptokinase does not increase the risk of hemorrhage.</p>		
<b>re-expansion pulmonary edema following fluid drainage</b>	<b>short term</b>	<b>low</b>
<p>This complication is more common when &gt;1.5 L of fluid is drained at one time in patients who have had lung collapse for at least 7 days.</p> <p>In adults, the drain should be clamped if the patient develops symptoms of cough or chest pain during initial drainage or once 1 to 1.5 L have been drained.</p> <p>In children, the drain should be clamped for 1 hour once 10 mL/kg of fluid have been drained.</p>		
<b>empyema necessitans</b>	<b>long term</b>	<b>low</b>
<p>Direct extension of the empyema through the chest wall is known as empyema necessitans and is preventable with prompt treatment of the empyema.</p> <p>Surgical debridement is indicated in the treatment of this complication.</p>		

Complications	Timeframe	Likelihood
<b>bronchopleural fistula</b>	<b>long term</b>	<b>low</b>
<p>Unrecognized empyema may extend internally into a bronchus forming a bronchopleural fistula and causing a pyopneumothorax.</p> <p>The majority of fistulae resolve with continued chest drainage and antibiotics, although surgery is sometimes necessary.[8]</p>		
<b>respiratory failure</b>	<b>variable</b>	<b>high</b>
<p>Acutely, if the volume of pleural fluid is large and drainage is difficult due to loculations or pus, restrictive ventilatory dysfunction may develop. Surgery or fibrinolytics should be considered in such cases.</p> <p>Chronically, the pleura may remain thickened, causing a restrictive pulmonary defect. In such cases, decortication should be considered.</p>		
<b>secondary scoliosis</b>	<b>variable</b>	<b>low</b>
<p>This complication is commonly seen on CXRs in children with empyema but is transient. Once its resolution has been confirmed on CXR, no treatment is required.</p>		

## Prognosis

Patient outlook is variable. Some patients respond fully to antibiotic treatment and chest drain insertion within a couple of weeks. However, approximately 24% do not respond and require surgery.[8] Most patients will recover fully, but a small number will develop chronic pleural thickening causing restricted ventilation or chronic pleural infection.

Mortality following empyema is approximately 15% to 20% and is higher in patients with significant comorbidities or immunocompromise.[3] [23]

Factors associated with a worse 3-month mortality include elevated serum urea, elderly age, nonpurulent effusion, hospital-acquired infection, and low serum albumin levels, collectively known as the RAPID [Renal (urea), Age, fluid Purulence, Infection source, Dietary (albumin)] score.[25] Of these variables, only elderly age has been associated with an increased need for surgery at 3 months. Although it seems counterintuitive that nonpurulent effusions would be associated with worse outcomes, this may be explained by the clinical observation that frankly purulent effusions appear to have less loculations and as a result are more likely to fully drain without the need for additional intervention such as intrapleural enzyme therapy or surgery.

### Outcome based on the American College of Chest Physicians categorization of parapneumonic effusions

Category 1 empyemas: free-flowing pleural effusion, <10 mm on lateral decubitus chest x-ray (CXR), thoracentesis (pleural aspiration) not required; a very low risk of poor outcome.

Category 2 empyemas: moderate free-flowing effusion (less than half of hemithorax), Gram stain and culture negative, pH >7.2; a low risk of poor outcome.

Category 3 empyemas: large or loculated pleural effusion or pleural thickening, or positive Gram stain or culture, or pH <7.2; a moderate risk of poor outcome.

Category 4 empyemas: aspiration of frank pus; a high risk of poor outcome.

### **Abnormalities on chest x-ray**

Although invariably abnormal at discharge, most CXR changes resolve within 3 to 6 months with some residual pleural thickening. A repeat CXR should be taken 4 to 6 weeks after discharge.

### **Impaired pulmonary function**

Some patients develop restrictive pulmonary function as a result of residual pleural thickening following chest tube removal. This pleural thickening resolves in most patients within several months and pulmonary function is usually near normal after 3 to 6 months. If reduced pulmonary function persists after 6 months and the patient is symptomatic, surgical decortication (a major thoracic operation involving the evacuation of pus and debris from the pleural space and removal of fibrous tissue from the visceral and parietal pleura) should be considered.



## Diagnostic guidelines

### International

**Practice parameter for specifications and performance of image-guided percutaneous drainage/aspiration of abscesses and fluid collections (PDAFC)** (<http://www.acr.org/Quality-Safety/Standards-Guidelines>) [30]

**Published by:** American College of Radiology; Society of Interventional Radiology; Society for Pediatric Radiology **Last published:** 2023

**Paediatric complicated pneumonia: diagnosis and management of empyema** (<http://www.cps.ca/en/documents>) [26]

**Published by:** Canadian Paediatric Society **Last published:** 2011 (updated 2018)

## Treatment guidelines

### International

**The American Association for Thoracic Surgery consensus guidelines for the management of empyema** (<https://www.ncbi.nlm.nih.gov/pubmed/?term=The+American+Association+for+Thoracic+Surgery+consensus+guidelines+for+the+management+of+empyema>) [8]

**Published by:** American Association for Thoracic Surgery **Last published:** 2017

**ACR Appropriateness Criteria: radiologic management of infected fluid collections** (<https://www.acr.org/Clinical-Resources/ACR-Appropriateness-Criteria>) [61]

**Published by:** American College of Radiology **Last published:** 2019

**Paediatric complicated pneumonia: diagnosis and management of empyema** (<http://www.cps.ca/en/documents>) [26]

**Published by:** Canadian Paediatric Society **Last published:** 2011 (updated 2018)

**EACTS expert consensus statement for surgical management of pleural empyema** (<http://ejcts.oxfordjournals.org/content/48/5/642.full>) [22]

**Published by:** European Association for Cardio-Thoracic Surgery **Last published:** 2015

**The British Thoracic Society Guideline for pleural disease** (<https://www.brit-thoracic.org.uk/quality-improvement/guidelines>)

**Published by:** British Thoracic Society **Last published:** 2023

## Key articles

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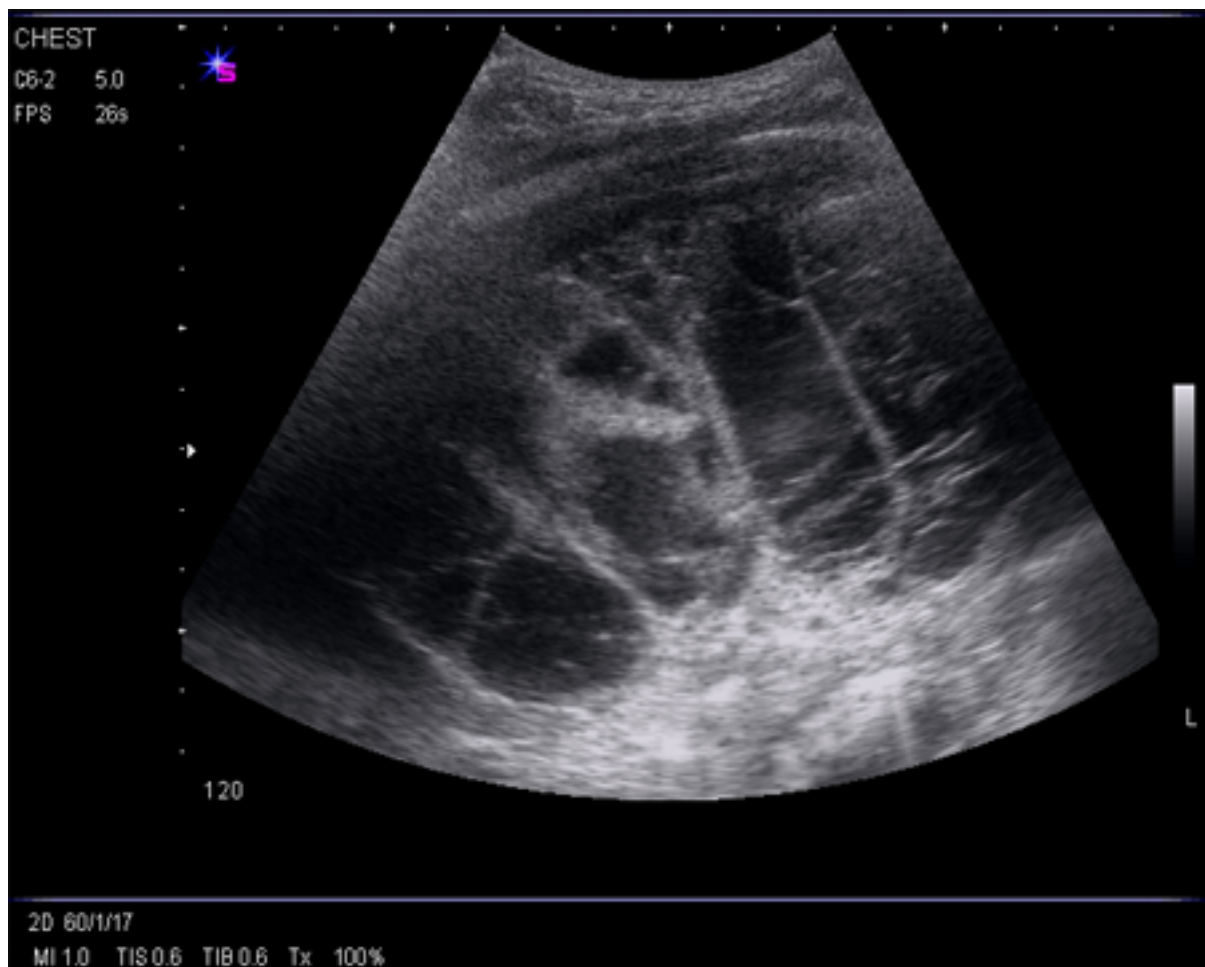


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## Images



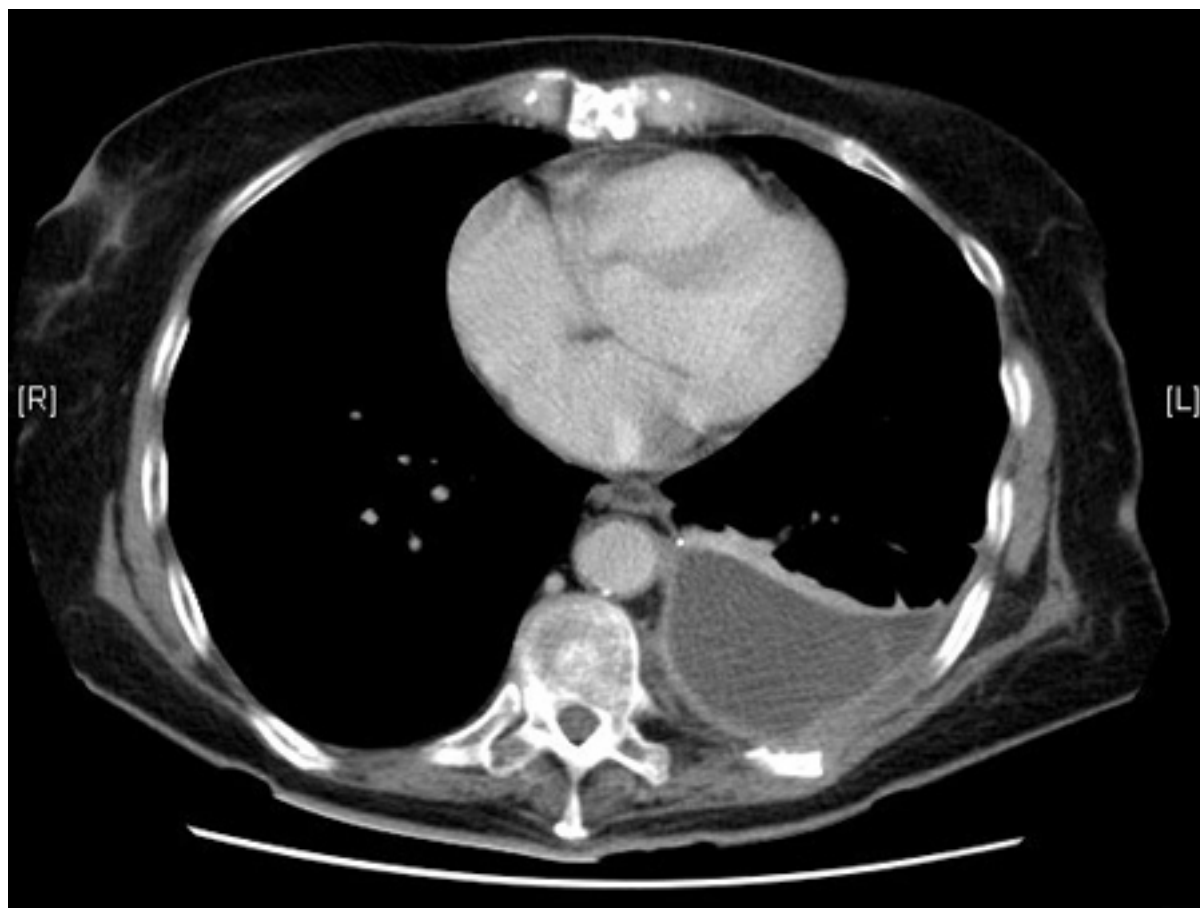
*Figure 1: Ultrasound image of heavily septated empyema*

*From the collection of Najib Rahman, RTU, Oxford*



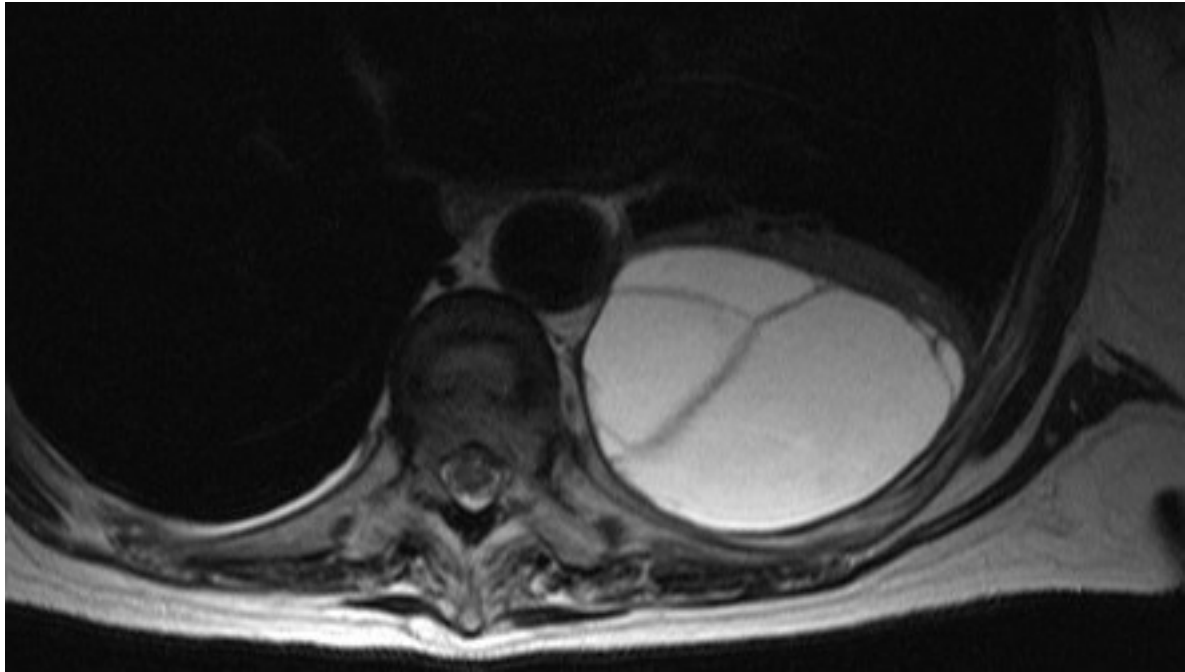
*Figure 2: CT scan of thoracic empyema*

*From the collection of Najib Rahman, RTU, Oxford*



*Figure 3: CT scan of thoracic empyema*

*From the collection of Najib Rahman, RTU, Oxford*



*Figure 4: MRI scan of septated empyema*

*From the collection of Najib Rahman, RTU, Oxford*

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## Interpretation of numbers

Regardless of the language in which the content is displayed, numerals are displayed according to the original English-language numerical separator standard. For example 4 digit numbers shall not include a comma nor a decimal point; numbers of 5 or more digits shall include commas; and numbers stated to be less than 1 shall be depicted using decimal points. See Figure 1 below for an explanatory table.

BMJ accepts no responsibility for misinterpretation of numbers which comply with this stated numerical separator standard.

This approach is in line with the guidance of the [International Bureau of Weights and Measures Service](#).

## Figure 1 – BMJ Best Practice Numeral Style

5-digit numerals: 10,000

4-digit numerals: 1000

numerals < 1: 0.25

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