

Pleural effusion

Summary

Pleural effusion is the abnormal accumulation of fluid in the pleural cavity between the lining of the lungs and the thoracic cavity (i.e., the visceral and parietal pleurae). Normally, a small amount of pleural fluid is present, which helps lubricate the pleural cavity and facilitates lung movement within the thoracic space. An imbalance between the oncotic and hydrostatic forces that govern pleural fluid formation and lymphatic drainage can result in excessive fluid accumulation. Fluid that permeates into the pleural cavity through intact pulmonary vessels, e.g., in congestive heart failure (CHF), is called a transudate. Conversely, fluid that escapes into the pleural cavity through lesions in blood and lymph vessels, e.g., due to inflammation or tumors, is called an exudate. Pleural effusion is often diagnosed using chest x-ray and ultrasound, but chest CT may be used for very small effusions. Thoracentesis serves as both a diagnostic and therapeutic procedure: pleural fluid analysis can help identify the underlying cause and excess pleural fluid evacuation can provide symptomatic relief. Treatment of pleural effusion often focuses on treating the underlying condition.

FEEDBACK

Definition:

An excessive amount of fluid between pleural layers that impairs the expansion of the lungs.

Etiology and Types:

Etiology

Fluid accumulates in the pleural space when the local hydrostatic forces that are pushing fluid out of the vascular space exceed the oncotic forces that are drawing fluid back into the vascular space. Pleural effusions can be transudates (intact membrane but abnormal hydrostatic or oncotic forces) or exudates (decreased integrity of the membrane due to inflammatory processes or impaired lymphatic drainage). There are relatively few causes of transudates, the primary ones being congestive heart failure and hypoproteinemia states, whereas the causes of exudates are numerous. Almost any pulmonary inflammatory process can result in pleural fluid accumulation. Among the most common causes of exudates are infection (e.g., tuberculosis, bacterial pneumonia), collagen vascular diseases (e.g., systemic lupus erythematosus), and malignancy. Chylous pleural effusions (elevated triglyceride levels) are seen with thoracic duct injury and abnormalities of lymphatic drainage (lymphangiomyomatosis, lymphangiectasia). Bacterial pneumonia can lead to an

accumulation of pleural fluid (parapneumonic effusion). When this fluid is purulent or infected, then it is called an empyema, although often the terms parapneumonic effusion and empyema are used interchangeably. Parapneumonic effusion/empyema is the most common reason for effusion in children. Upright and decubitus chest radiograph (Fig. 138.1) can be useful for identifying parapneumonic effusion; however, chest ultrasound or CT is necessary for accurate estimates of fluid volume and organization (loculation) if surgical drainage is being considered. Most parapneumonic effusions are due to pneumonia caused by *Streptococcus pneumoniae*, group A streptococci, or *Staphylococcus aureus*.

Transudative effusions [2][3]

- Congestive heart failure
- Hepatic cirrhosis
- Nephrotic syndrome
- Protein-losing enteropathy
- Chronic kidney disease (Na^+ retention)
- Rare causes
 - Superior vena cava obstruction
 - Myxedema

Exudative effusions [2][3]

- Infection
 - Pneumonia (parapneumonic effusion)
 - Tuberculosis
 - Pleural empyema
 - Parasitic illness (e.g., amebiasis, echinococcal disease)
- Malignancies
 - Lung cancer
 - Metastatic breast cancer
 - Lymphoma
 - Mesothelioma
 - Ovarian cancer
- Pulmonary embolism (PE)
- Autoimmune disease (especially collagen vascular diseases)
 - Vasculitis
 - SLE
 - Rheumatoid arthritis
 - Sarcoidosis
- Trauma (high vascular permeability)
- Pancreatitis
- Hemothorax
- Chylothorax
- Pseudochylothorax
- Rare causes
 - Postcardiac surgery
 - Esophageal perforation
 - Gynecological causes
 - Endometriosis
 - Ruptured ectopic pregnancy
 - Meigs syndrome

Transudative vs exudative pleural effusion ^{[1][2][3]}			
		Transudative pleural effusion	Exudative pleural effusion
Pathophysiology 🗨		• ↑ Capillary hydrostatic pressure (increased <u>capillary</u> wedge pressure) • ↓ <u>Capillary oncotic pressure</u>	• ↑ Capillary permeability (e.g., due to inflammation)
Common causes (See “Etiology of pleural effusion” for details.)		• <u>Congestive heart failure</u> • Low protein states, e.g., chronic <u>kidney</u> and <u>liver</u> disease	• Pulmonary infections • <u>Malignancy</u> of pulmonary or metastatic origin • Inflammatory conditions: e.g., pancreatitis, autoimmune diseases • Injury: e.g., <u>hemothorax</u>, <u>chylothorax</u> • <u>Pulmonary embolism</u>
Light Criteria	Pleural fluid protein/serum protein ratio	• ≤ 0.5	• > 0.5
	Pleural fluid LDH/serum LDH ratio	• ≤ 0.6	• > 0.6
	Pleural fluid LDH	• < ⅔ the upper limit of normal serum <u>LDH</u>	• > ⅔ the <u>upper limit of normal serum LDH</u>

Notes:

- Infection producing a reactive **parapneumonic effusion** or a more serious purulent **empyema** is the most common cause of pleural effusion in children.
- Empyema often is caused by:
 1. *Streptococcus pneumoniae*
 2. group A streptococci
 3. *S. aureus*
 4. rarely by *Mycobacterium tuberculosis*, *Mycoplasma*, or adenovirus.
- Anaerobic bacteria produce empyema associated with aspiration pneumonia and dental, lung, or subdiaphragmatic abscesses.
- *H. influenzae* frequently causes parapneumonic effusion but is rare in immunized populations.

Clinical findings:

Small pleural effusions may be asymptomatic, but if they are large enough to compress lung tissue, then they can cause dyspnea, tachypnea, and occasionally chest pain. Effusions due to infection are usually associated with fever, malaise, poor appetite, pleuritic chest pain, and splinting. Physical findings include tachypnea, decreased breath sounds, dullness to percussion, and decreased tactile fremitus. Large effusions may occupy more than half the hemithorax and cause a mediastinal shift away from the affected side, compromising respiratory status, particularly in young children.

Symptoms [3]

- Patients with a small pleural effusion (≤ 300 mL) are often asymptomatic. 🗨
- Characteristic symptoms
 - Dyspnea 🗨
 - Symptoms of hypoxia
 - **Pleuritic chest pain** (sharp retrosternal pain) 🗨
 - Dry, nonproductive cough 🗨
 - Symptoms of the underlying disease (e.g., fever in empyema, cachexia in cases of malignancy, symptoms of left-sided heart failure)

Physical exam findings

- Inspection and palpation
 - **Asymmetric expansion** and **unilateral lagging on the affected side**
 - **Reduced tactile fremitus** due to fluid in the pleural space 🗨
- Auscultation
 - Faint or absent **breath sounds** over the area of effusion
 - **Pleural friction rub** (squeaking sound of inflamed pleural layers rubbing together during inspiration and expiration) 🗨
- Percussion: **dullness** over the area of effusion 🗨

Tactile fremitus
A part of the pulmonary examination used to evaluate the conduction of vibrations to the chest wall produced during speech. Palpate the posterior or chest wall with the distal aspects of both hands while the patient says a phrase such as "ninety-nine". Fremitus becomes more pronounced in the presence of consolidation and less pronounced in the presence of effusion or pneumothorax. The examiner can also assess fremitus with a stethoscope on the chest wall (vocal fremitus).

Diagnosis:

Approach

- Imaging is necessary to confirm the diagnosis.
- Consider diagnostic thoracentesis if the diagnosis is uncertain or management requires additional information (e.g., culture, cytology).
- Consider additional diagnostic procedures (e.g., bronchoscopy, VATS) if the diagnosis remains unclear.

Chest x-ray for pleural effusion [4][5]

- **Indications**
 - Standard initial imaging modality for detecting pleural effusion. 🗨
 - **Lateral decubitus view** (most sensitive): allows for detection of fluid collections as small as 5 mL 🗨 [6]
- **Supportive findings**
 - Typically unilateral **blunting of the costophrenic angle** 🗨 🗨
 - Homogeneous density with a **meniscus-shaped margin (meniscus sign)** 🗨
 - **Large effusion**
 - Complete opacification of the lung 🗨
 - **Mediastinal shift**
 - **Tracheal deviation away from the effusion** (space-occupying lesion)
 - Disease-specific signs: See "Pleural empyema", "Lung cancer", "Active primary tuberculosis", "Pneumonia diagnostics", and "Pneumothorax."

Supine CXR has poor sensitivity for pleural effusions, and effusions < 200 mL may not be visible on frontal upright CXR. Include lateral upright and lateral decubitus views whenever possible when obtaining radiographs. [6][3][4]

False positives for pleural effusions on CXR include elevated hemidiaphragm, atelectasis, consolidation, mass lesions.

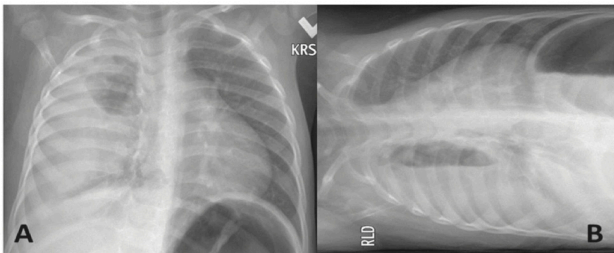
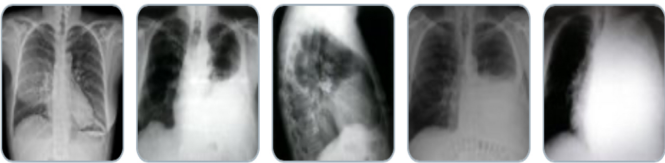


FIGURE 138.1 Parapneumonic effusion. A, Posterior-anterior chest radiograph showing dense opacification of the right hemithorax. B, On decubitus view, some of the density forms a horizontal layer indicating that there is pleural fluid in addition to pneumonia.



Thoracic ultrasound for pleural effusion [4][7]

• Indications

- Quick bedside assessment
- Thoracentesis planning

• Procedure: See "Lung POCUS" and "eFAST."

- **Ultrasound findings suggestive of pleural effusion:** hypoechoic or anechoic collection in the lower margins of the pleural cavity (costodiaphragmatic recess) 
- Very sensitive: can detect fluid amounts as low as 20 mL
- Hemothorax and empyema may appear heterogeneous.
- Pleural fluid septations may be present. 
- Allows for detection of pleural thickening and pleural nodules

 Thoracic ultrasound is more sensitive than chest x-ray for diagnosing effusions and estimating effusion size. [8]

 False positives on ultrasound can result if the following are mistaken for pleural fluid: subdiaphragmatic fluid (e.g., ascites), pericardial fluid, contained fluid (e.g., hypoechoic masses, abscesses), or pleural thickening. False negatives may result if clotted blood or empyema fluid is mistaken for normal lung or liver tissue. [9]

Chest CT [4][7]

- **Indications:** gold standard for small effusions but use is limited because of radiation and contrast exposure

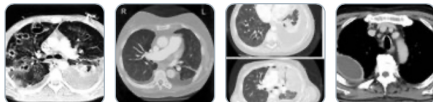
- Guiding placement of indwelling pleural catheters
- Directed thoracentesis of a loculated effusion
- Suspected parenchymal or pleural pathology
- Better quantification of the amount of fluid (compared to CXR) is desired

- **Procedure:** chest CT without IV contrast is usually sufficient

- With IV contrast: allows for the detection of underlying malignancy (e.g., metastases and/or primary tumor) 
- CT angiogram: helps to identify vascular pathology (e.g., dissection or AVM)

- **Supportive findings** 

- Can detect > 3–5 mL of fluid
- Fluid density measurement can help differentiate pleural effusion from empyema and hemothorax  [10]
- Disease-specific signs: See "Pleural empyema."



Diagnostic thoracentesis [3][11]

Can be combined with therapeutic thoracentesis if both are indicated. See "Thoracentesis" for detailed indications, contraindications, procedural steps, and complications.

- **Goal:** obtain samples for pleural fluid analysis, e.g., to differentiate transudates from exudates, and identify the underlying cause of pleural effusion

- **Indications** include new unilateral pleural effusions and bilateral effusions with atypical features (e.g., fever, chest pain, variable size).

• Routine pleural fluid studies

- Biochemistry: protein, LDH, pH, and glucose
- Gram stain and culture
- Cytology 

- **Serum studies** (for comparison): serum protein, LDH, pH, and glucose

• Advanced pleural fluid studies (case by case)

- Cell count 
- Lipids: cholesterol, triglycerides 
- Amylase, lipase 
- TB testing: adenosine deaminase, AFB smear microscopy
- Parasitology
- Tumor markers
- Rheumatological markers 
- NT-proBNP 

- **Laboratory studies:** may be indicated further workup of transudative effusions.

- Elevated serum NT-proBNP: suggests heart failure
- ↑ Liver transaminases, ↓ serum albumin, and abnormal coagulation studies: suggests cirrhosis
- Proteinuria: suggests nephrotic syndrome
- ↑ Serum TSH: suggests hypothyroidism

- **Invasive tests:** Consider for patients with inconclusive pleural fluid analysis to rule out malignancy or intracellular infection.

- Bronchoscopy
- Percutaneous needle biopsy
- VATS

TABLE 138.1	Pleural Fluid Analysis
EXUDATIVE EFFUSION BY LIGHT'S TRADITIONAL CRITERIA	
Pleural fluid protein/serum protein ratio >0.5 OR	
Pleural fluid LDH/serum LDH ratio >0.6 OR	
Pleural fluid LDH >two thirds the upper limits of laboratory's normal serum LDH	
CHYLOTHORAX	
Triglycerides >110 mg/dL	
TUBERCULOUS	
Positive acid-fast bacilli stain, culture	
Pleural fluid protein >4 g/dL	
Pleural fluid adenosine deaminase level >35-50 U/L	
Pleural fluid glucose 30-50 mg/dL	
HEMOTHORAX	
Pleural fluid hematocrit/serum hematocrit >0.5	

Pleural fluid analysis:

Differentiating transudates from exudates [6][12][7][3][13]

Primary pleural fluid analysis			
Laboratory parameters		Transudative effusion	Exudative effusion
Light criteria	Pleural fluid protein/serum protein ratio	• ≤ 0.5	• > 0.5
	Pleural fluid LDH/serum LDH ratio	• ≤ 0.6	• > 0.6
	Pleural fluid LDH	• $< \frac{2}{3}$ the upper limit of normal serum LDH	• Pleural fluid LDH $> \frac{2}{3}$ the upper limit of normal serum LDH • Very high LDH levels, e.g., > 1000 U/L, suggest empyema, malignancy, or rheumatoid effusion.
Pleural fluid cholesterol		• < 45 mg/dL	• > 55 mg/dL
Pleural fluid LDH		• < 200 U/L	• > 200 U/L
Pleural fluid cholesterol:serum cholesterol ratio		• < 0.3	• > 0.3

Light criteria are useful for **ruling out** an exudate if all criteria are assessed as the sensitivity is high. They are less reliable for **ruling in** an exudate as the specificity is poor and can misclassify ~ 25% of transudates as exudates. Interpret results taking the full clinical picture into account. [6][14]

Adjunctive pleural fluid analysis [3][7][13]

Pleural fluid parameter	Suggests transudative effusion	Suggests exudative effusion
Physical appearance	• Clear fluid • Does not froth or form clots	• Cloudy or straw-colored fluid (may be hemorrhagic in rare cases) • Froths when shaken and forms clots when left standing
Specific gravity	• ≤ 1.016	• > 1.016
pH Normal pH ~ 7.6	• 7.4–7.55	• < 7.3 –7.45
Glucose	• ≥ 60 mg/dL	• < 60 mg/dL
Total protein gradient (i.e., the difference between pleural fluid and serum total protein)	• > 3.1 g/dL lower than serum total protein	• < 3.1 g/dL lower than serum total protein
Albumin gradient	• > 1.2 g/dL lower than serum albumin	• < 1.2 g/dL lower than serum albumin

Differential Diagnosis:

- **Lung densities on imaging**
 - Lung mass, e.g., bronchial carcinoma, lung metastasis
 - Pneumonia
 - Interstitial lung disease
 - Atelectasis
- **Pleural densities on imaging**
 - Metastatic disease
 - Pleural fibrosis or scarring
 - Pleural mesothelioma
- **Other mimics**
 - Subphrenic abscess
 - Pneumothorax
 - Diaphragmatic hernia^[17]

Differential diagnosis of exudative effusions

Pleural fluid parameter		Associated conditions ^{[11][2][15]}
Cell count and differential	WBC count > 10,000 cells/mm³	• Parapneumonic effusion • Pancreatitis • Pulmonary embolism • Collagen vascular disease
	Neutrophils > 50% of total leukocytes	• Acute infection • Pulmonary infarct
	Lymphocytes > 50% of total leukocytes	• Primary or chronic tuberculous infection • Malignant effusion • Chylothorax
	RBC count > 5,000 cells/μL	• Hemothorax • Malignant effusion (i.e., bleeding tumor) • Pulmonary embolism/infarct
Hematocrit > 0.5 $\times$ peripheral hematocrit		• Hemothorax
pH < 7.2^[15]		• Complicated parapneumonic effusion • Empyema • Malignant effusion • Esophageal perforation • Collagen vascular disease
Glucose < 60 mg/dL		• Malignant effusion • Parapneumonic effusion • Empyema • Rheumatoid pleurisy • Tuberculous pleurisy • Esophageal rupture • Lupus pleuritis
Positive Gram stain or culture		• Parapneumonic effusion • Empyema
Adenosine deaminase > 50 mcg/L Positive AFB smear microscopy		• Tuberculous effusion
Abnormal cytology		• Malignant effusion
Amylase > 200 mcg/dL		• Pancreatitis • Malignant effusion • Esophageal perforation • Ruptured ectopic pregnancy
Positive rheumatoid factor, ANA		• Collagen vascular diseases

Lipids	Triglycerides > 110 mg/dL	- Chylothorax - Tuberculous effusion - Accidental intrathoracic leak of TPN solution
	Total cholesterol > 200 mg/dL Total cholesterol:triglyceride ratio > 1 Cholesterol crystals	Pseudochylothorax
	Total cholesterol 55–200 mg/dL Chylomicrons and fat-soluble vitamins	Chylothorax
Appearance	Cloudy, milky	- Chylothorax - Pseudochylothorax
	Purulent	- Parapneumonic effusion - Empyema
	Bloody	- Hemothorax - Malignant effusion - Pulmonary embolism/infarct

Management:

TREATMENT

- Therapy is directed at the underlying condition causing the effusion and at relief of the mechanical consequences of the fluid collection.
- small effusions, especially if they are transudative, no drainage therapy is required.
- For large effusions, drainage with a chest tube, especially if the fluid is purulent (empyema), is often needed.
- In cases of empyema and parapneumonic effusion, in which drainage is complicated by a loculated pleural collection, video-assisted thoracoscopic surgical débridement is useful and may reduce morbidity and length of hospital stay.
- small - moderate parapneumonic effusions can be managed conservatively with IV antib.
- If the underlying condition is treated successfully, the prognosis for pediatric patients with pleural effusions, including empyema, is excellent.

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