

Pleural Effusion — Diagnoses, Treatment, Transudate and Exudate

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Medical students often encounter patients with pleural effusion during internships and their residency. These patients do not always suffer from dyspnea and an accurate clinical examination is crucial for the diagnosis. In oral and written exams, explaining the difference between transudate and exudate is a frequent task. In this article, you can find all the important information regarding pleural effusion - for clinical practice and your studies!



Definition of Pleural Effusion

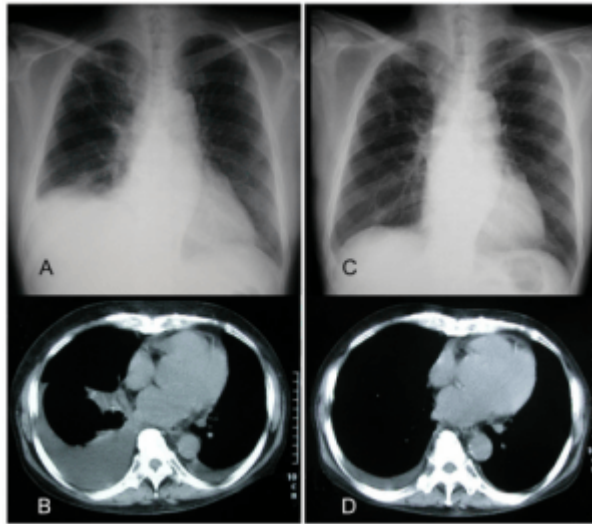


Image: "Successful management of refractory pleural effusion due to systemic immunoglobulin light chain amyloidosis by vincristine adriamycin dexamethasone chemotherapy" by J Med Case Rep (2010). License: [CC BY 2.0](https://creativecommons.org/licenses/by/2.0/)

Pleural effusion as an accumulation of fluid in the pleural cavity

Pleural effusion refers to a pathological accumulation of pleural fluid in the pleural cavity that has been caused by either an inflammation (**pleuritis**) or other diseases.

Pleural fluid is physiologically produced at the capillary bed of the parietal pleura and absorbed by the parietal pleural lymphatics and visceral pleura.

Pathology of Pleural Effusion

Pleural effusion: Transudate and exudate

Depending on the **overall protein concentration** of the pleural effusion, a distinction is made between **transudate** (< 30 g/l) and **exudate** (> 30 g/l).

Transudate is a clear fluid containing few cells. It can emerge, e.g., as a consequence of stasis: due to the increased **hydrostatic pressure**, the fluid efflux from the capillaries increases. Or the **colloid osmotic pressure** in the **vessels** may be **decreased** (e.g., in the event of **hypoalbuminemia**), causing more fluid to leak.

Exudate, on the other hand, is rich in cells and is mostly a consequence of **inflammations** or **tumor diseases**. Here, the capillary walls' permeability for tumor cells, plasma proteins, and other **blood components** increases (**barrier dysfunction**). These particles will then form part of the pleural effusion, which is why exudate has such high content of **cells** and proteins.

In both cases, an increase in **lymph production** can also be observed. This increased production then exceeds the maximum re-absorption capacity of the pleura and, thus, also contributes to the increased fluid accumulation.

At a glance: Study aid for the differentiating criteria of

both forms of pleural effusion

	Overall protein concentration	Quotient: $\frac{\text{protein}_{\text{effusion}}}{\text{protein}_{\text{serum}}}$	LDH	Quotient: $\frac{\text{LDH}_{\text{effusion}}}{\text{LDH}_{\text{serum}}}$
Transudate	< 30 g/l	< 0.5	< 200 U/l	< 0.6
Exudate	> 30 g/l	> 0.5	> 200 U/l	> 0.6

The most telling parameters are the protein and LDH quotients. Thus, the following applies: If one of these parameters is elevated (> 0.5 or > 0.6), the fluid is considered exudate.

Special forms of pleural effusion

Special forms of pleural effusion are the **chylothorax** and the **hematothorax**. The first one consists primarily of **lymphatic fluid**, the pleural effusion is milky and cloudy with a markedly elevated **triglyceride content** (> 110 mg/dl). A hematothorax is basically an accumulation of blood.

Note: A bloody pleural effusion has to be considered suspicious for a tumor until proven otherwise.

Etiology of Pleural Effusion

Causes of pleural effusions

The three most frequent causes of transudate are:

- Lung embolism
- Decompensated left cardiac insufficiency
- Liver cirrhosis

For exudate, **pneumonia**, **malignomas**, and also **lung embolism** should be mentioned. So the latter can cause both transudate and exudate. In addition, causes are an increased rate of formation, a decreased rate of absorption, and direct extension from the peritoneum. **Tuberculosis** is the most frequent cause of pleural effusion in patients under the age of 40!

Study aid: The most important causes of pleural effusion

	Causes
Transudate	Increased hydrostatic pressure: decompensated cardiac insufficiency, lung embolism, venous congestion
	Decreased colloid osmotic pressure: liver cirrhosis, hypoalbuminemia, nephrotic syndrome, uremia, exudative enteropathy
Exudate	Malignant: bronchial carcinoma (40 %), metastases (carcinoma of breast 25 %, gastrointestinal 5 %, ovarian carcinoma 5 %), malignant lymphomas (10 %), pleural mesotheliomas
	Infectious: pneumonia, tuberculosis
	Rheumatic: lupus erythematosus, rheumatoid arthritis
	Others: lung embolism, pancreatitis, pericarditis, endometriosis

Chylothorax	Shifting or lesions of the thoracic duct by tumors/metastases, trauma, or iatrogenic
Hemothorax	Trauma, iatrogenic (after biopsies or punctures), aortic aneurysm rupture, pleural malignomas

Symptoms of Pleural Effusion

Dyspnea is the cardinal symptom of pleural effusion

Besides symptoms that are due to accompanying or underlying diseases, **dyspnea** is the only direct symptom. This shortness of breath can be more or less pronounced, depending on the severity of the effusion.

Diagnostics of Pleural Effusion

Anamnesis and clinical examination of pleural effusions

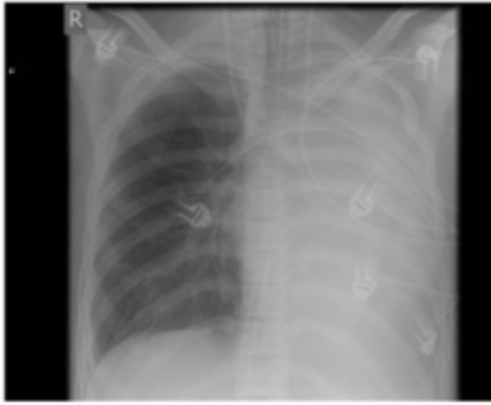
As always, anamnesis is the first step in the diagnostic process for pleural effusion. Especially the different possible **etiologies** have to be considered (tumor in medical history? risk factors for lung embolism? etc.).

In the clinical examination, an asymmetrical chest expansion, with delayed expansion on the side of the effusion, can be noticed. **Auscultation** presents decreased or inaudible breath sounds over the effusion. Sometimes, **bronchial breath sounds** can be heard over the lung parts directly above the effusion because the lung is consolidated, i.e. compressed, here.

Also, **bronchophony** can be absent over the pleural effusion since the vibration is being reflected at the line between lung tissue and pleural effusion (two matters of different density) and is, thus, not conducted to the hand of the examiner. In the case of an effusion > 300 ml, chest examination will also be notable for dullness to **percussion**. The upper border of this dullness follows a laterally ascending curve (**Ellis-Damoiseau line**). **Palpation** of larger effusions is notable for a **reduced fremitus** over the affected side due to the same reasons why bronchophony is absent.

Imaging of pleural effusion

If the torso is erected, the effusion follows gravity and accumulates on the costophrenic angles of the pleural spaces (**costodiaphragmatic recess**). The most sensitive and gentle way to confirm a pleural effusion diagnosis is **sonography** while the patient is sitting down. This way, effusions with a volume of **20 ml** or more will be depicted as an **anechoic** (= dark) area. Sonographic imaging also allows for the assessment of the pleura (fibrosis? tumor?) and the organization of the effusion, as well as for identifying a suitable site for puncture.



(A)



(B)

Image: "Bedside lung ultrasound in the critically ill patient with pulmonary pathology" by Crit Ultrasound J (2012). License: [CC BY 2.0](https://creativecommons.org/licenses/by/2.0/)

Chest x-rays for diagnosing pleural effusions can be made in different positions and planes:

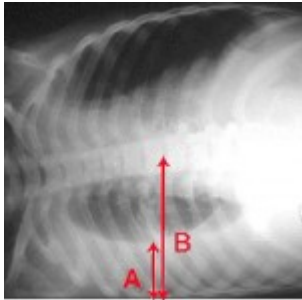

Position and Plane	Limit of Detection	Example
Lateral decubitus (with the affected side facing down)	100 ml	<p>Chest x-ray in lateral decubitus position with evidence of a pleural effusion:</p> 
Erect (lateral projection)	150 ml	<p>Especially the recesses are well visible since they reach down furthest on the dorsal side.</p>
Erect (PA projection)	200 ml	<p>Pleural effusion left and right with bilateral shadowed costophrenic angles:</p> 

Image: "Medical X-rays." by © Nevit Dilmen. License: [CC BY 2.0](https://creativecommons.org/licenses/by/2.0/)

In x-ray images, the effusion is depicted as a **homogenous shadow**, which sometimes ascends laterally (**crescent sign**). When the patient is standing, this shadow is usually seen in the lowest costodiaphragmatic recesses. Furthermore, the **diaphragm** is usually **difficult to identify**. An **extensive decrease in transparency** of the entire lung is possible as well as a **mediastinal shift** to the opposing side. In rare cases, **atypical localizations** of the effusion may be found: for example, encapsulated and intralobular (DD: round lesion) or encapsulated in the area of pleural adhesions.

Left pleural effusion with mediastinal shift to the opposing side:



Image: "Mediastinalshift nach rechts bei sehr grossem Pleuraerguss links." by Hellerhoff. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

Thoracic CT scans will typically performed as part of advanced diagnostic procedures when the etiology is unclear. It allows for the detection of the smallest amounts of effusion, which will be notable as sickle-shaped consolidations between lung and thoracic wall.

Thoracic CT with distinct pleural effusion, right:



Image: "Pleuraerguss in der Computertomographie axial Weichteilfenster rechte Pleurahöhle" by Hellerhoff. License: [CC BY-SA 3.0](https://creativecommons.org/licenses/by-sa/3.0/)

Pleural puncture: Diagnostics and treatment

For the purposes of differential diagnosis, obtaining testing material through a puncture of the pleural effusion is an important step. This applies in particular to any case of a **first or etiologically unclear** pleural effusion.

For this procedure, the patient is **sitting** down, a **local anesthetic** is applied, and the puncture needle is inserted dorsally into the area of the effusion, but not below the 9th

rib (to avoid sub-diaphragmatic injuries). It is crucial to insert the needle at the upper edge of the rib as to prevent any injuries to the nerves and vessels at the inferior edge of the rib. In cases of encapsulated effusions or atypical localizations, the finding of the puncture site should be assisted **sonographically**.

The material obtained from the puncture should be stored in **four tubes**:

1. The first tube is for **microbiology**. From this material, a **bacterial culture** is made in order to perform a **Gram stain** and, in case of suspected tuberculosis, a **Ziehl-Neelsen stain**. This tube has to be kept sterile at all times!
2. The second tube is for **clinical chemistry**. With this material, various parameters will be determined: cell count (e.g., lymphocytosis for cases of tuberculosis, sarcoidosis), **pH level** and **glucose** (diminished glucose levels and an acidic pH suggest an inflammatory or malignant genesis), **triglyceride** (elevated in case of a chylothorax), **amylase** and **lipase** (elevated in case of a pancreatic effusion caused by pancreatitis, **pancreas** carcinoma, or others), and specific **tumor markers** in case of a suspected tumor disease.
3. The third tube is for **pathology**. Here, a **cytological smear** is prepared for evaluation of malignancy. Indications for malignancy would include, inter alia, a **shift in the nucleus-plasma relation**, many **mitoses**, and **multinucleated cells**.
4. A fourth tube is kept for other, not yet foreseeable examinations.

Macroscopically, a first assessment of the punctured effusion can be made:

Serous	Bright, clear, "amber" fluid: mostly transudate with few cells
Hemorrhagic	Reddish: bloody transudate or exudate – trauma or malignoma?
Chylous	Milky and cloudy: chylothorax
Purulent	Yellowish and dull: exudate in cases of pleural empyema, tuberculosis, or abscesses

The puncture furthermore represents a relief for the patient and can thus be considered a part of **symptomatic treatment**, especially in cases of severe dyspnea due to lung compression and cardiopulmonary strains due to a mediastinal shift, i.e., in very severe cases of pleural effusions.

Note: Every pleural puncture should be followed by a chest x-ray to exclude an iatrogenic pneumothorax!

Treatment of Pleural Effusion

Pleural draining and pleurodesis

Treating the underlying disease should be the focus of any treatment approach. When this is followed through, transudates will most likely resolve completely.

As explained in the section on diagnostics, larger effusions with severe dyspnea are therapeutically punctured in order to relieve the patient from his/her shortness of breath. However, **never extract more than 1.5 liters** in a single session since there is the risk of **re-expansion edema** or great losses of protein. Therefore, for larger effusions, treatment consists of **suction drainage** over the course of several days.

If the pleural effusion is **recurrent** (especially in cases of malignant genesis) and/or cannot be controlled with medication, **chemical pleurodesis** can be performed. After the puncture of the effusion, a fibrosing substance (e.g., **talcum**) is introduced into the

pleural cavity through the chest drain. The substance triggers an inflammatory reaction that causes the two pleural layers to adhere to each other and, thus, prevents any further accumulation of fluids in the pleural cavity.

For a well-aimed **biopsy** and the isolation of **histological tissue samples** in cases of malignant effusions, and also for further bacteriological diagnostics of non-controllable para pneumatic effusions and pleural empyema, an additional **video-assisted thoracoscopy** may be performed as well.

Complications of Pleural Effusion

Pleural fibrosis and pleural empyema

Sometimes, a pleural effusion is followed by the formation of **pleural fibrosis**. This manifests as cicatricially altered, mostly thickened adhesions of the pleurae.

If the pleural effusion is the result of pneumonia, it is called a **parapneumonic effusion**. These particularly tend to become **infected** and are then further classified, using various parameters, as **uncomplicated** (= not infected), **complicated** (= infected), or **pleural empyema** (= purulently infected).

	Puncture Specimen	Detection of Bacteria	Leucocytes	pH
Uncomplicated	Clear	Sterile	+	> 7,3
Complicated	Cloudy	(+)	++	7,1 - 7,2
Pleural Empyema	Purulent	+	+++	< 7,1

Review Questions

Solutions can be found below the references.

1. Which statement concerning the diagnostics in the context of pleural effusion is correct?

- A. Pleural effusions of more than 500 ml can be detected sonographically.
- B. Chest x-ray with lateral projection is the most sensitive detection method.
- C. For etiological assessments, a thoracic CAT scan should always be performed.
- D. One tube puncture specimen is for microbiological tests.
- E. Auscultation is notable for wheezing and buzzing sounds.

2. In which aspect does a transudate differ from exudate?

- A. LDH concentration of exudate is higher.
- B. The overall protein concentration of transudate is higher.
- C. The quotient $\text{LDH}_{\text{effusion}}/\text{LDH}_{\text{serum}}$ in exudate is < 0.6.
- D. The quotient $\text{protein}_{\text{fluid}}/\text{protein}_{\text{serum}}$ in transudate is > 0.5.
- E. Exudate usually develops as a result of increased hydrostatic pressure.

3. Which of the following diseases is least likely to cause a pleural effusion consisting of transudate?

- A. Decompensated cardiac insufficiency
- B. Lung embolism
- C. Nephrotic syndrome

- D. Liver cirrhosis
- E. Bronchial carcinoma

References

A. Tremblay, C. Mason, G. Michaud: Use of tunneled catheters for malignant pleural effusions in patients fit for pleurodesis. In: [The European Respiratory Journal](#), 2007

Correct Answers: 1D, 2A, 3E

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