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Diagnostic Approach to Pleural Effusion

Objectives

- Define the leading causes of pleural effusion
- Classify the type of effusion
- Identify procedures and tests associated with diagnosis

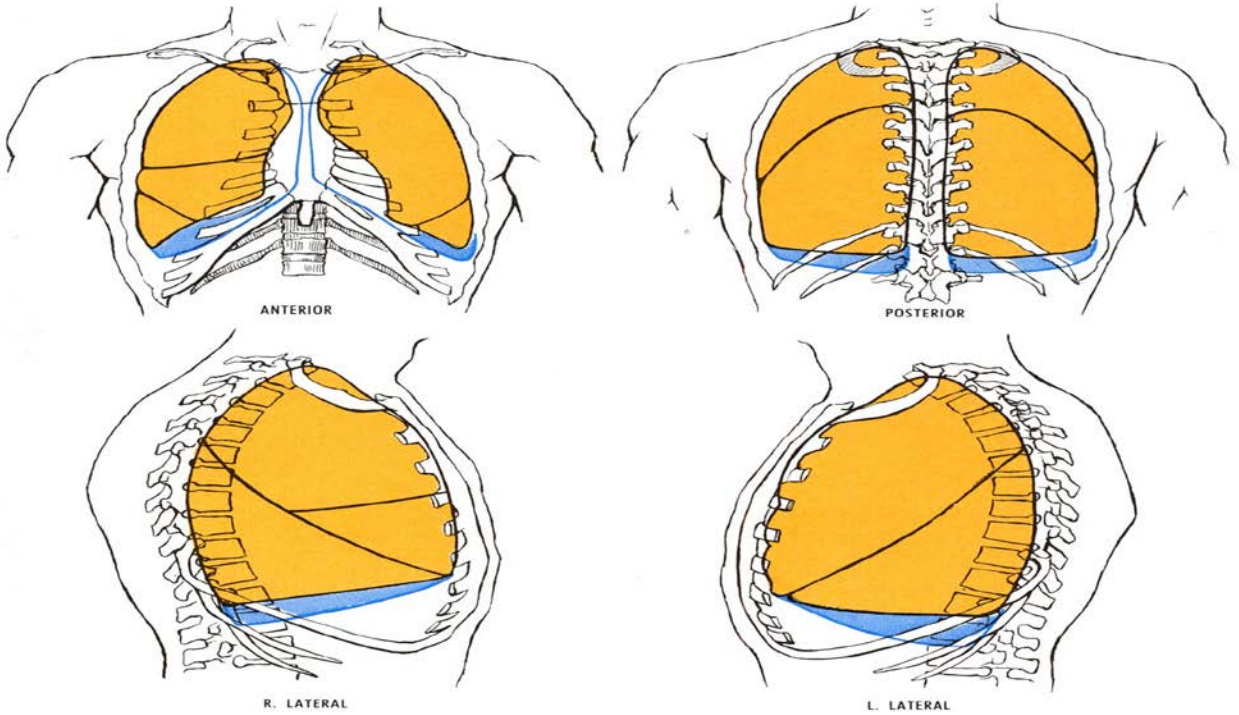
Agenda

- Basic anatomy of the lungs
- What is pleural fluid?
- Types of pleural effusions
- Diagnostic tools for determining pleural effusion
- Importance of pleural fluid pH measurement
- Proper sample handling and test methods for pleural fluid analysis
- Summary

Each year in the **United States** , an estimated 1.5 million people a year develop **pleural effusions**....

https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4428160/

Basic Anatomy of the Lungs



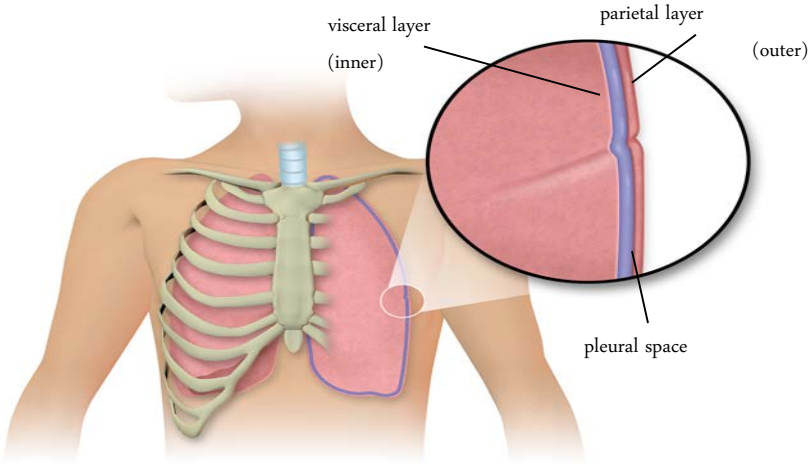
Curr Opin Pulm Med. Jul 2001;7(4):180-2.

What is Pleura?

Pleura is a moist, double-layered membrane that surrounds the lungs and lines the rib cage.

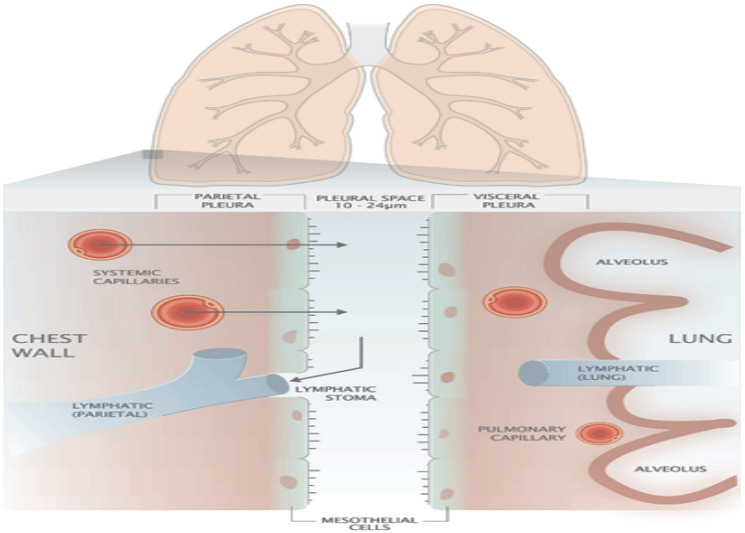
Pleura consists of two layers:

- ***Visceral layer*** which is adherent to the lung (pulmonary pleura)
- ***Parietal layer*** which lines the inner aspect of the chest wall, diaphragm and sides of the pericardium and mediastinum (costal pleural)



http://medical-dictionary.thefreedictionary.com/pleural+effusion

What is Pleural Fluid?



- Thin film of liquid that fills the pleural space and acts as a lubricant
- Pleural fluid allows for the lung and the chest wall to slide with respect to each other during respiration
- Constantly renewed
- In healthy individuals, the volume of pleural fluid surrounding each lung is approximately 10mL (adult weighing 165 pounds)

Critical Care & Pain 2007; 7: 10-14
Am J Respir Crit Care Med 2000; 162: 1023-26

What is a Pleural Effusion?

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Pleural Effusion:

- An abnormal collection of fluid in the pleural space resulting from excess fluid production or decreased absorption.
- Requires urgent evaluation and treatment.

- **Signs and Symptoms of a pleural effusion:**
  - The additional fluid puts pressure on the lungs, reducing their ability to move freely.
  - A large amount of pleural fluid may cause shortness of breath.
  - In some cases of pleural effusion, this excess liquid causes an infection of the pleura.
  - Typically, the patient experiences:
    - Shortness of breath (dyspnea)
    - Chest pain
    - Gastric discomfort (dyspepsia)
    - Cough

http://medical-dictionary.thefreedictionary.com/pleural+effusion
Compr Ther. Winter 2007;33(4):237-46.

A Pleural Effusion is NOT a disease

- It is important to recognize that a pleural effusion is not a disease
- A pleural effusion is a result of many different diseases

Transudative Effusion

Caused by fluid leaking into the pleural space due to increased pressure, or low protein content, in the blood vessels

- **Congestive heart failure**
- Cirrhosis
- Nephrotic Syndrome
- Hypoalbuminemia
- Hypothyroidism

Exudative Effusion

Caused by inflammation, blocked blood vessels, lung injury, drug reactions

Infection

Pulmonary Embolism

Malignant diseases

Autoimmune disease

Pancreatitis

Esophageal rupture

Post CABG

Post MI

Drug induced

http://medical-dictionary.thefreedictionary.com/pleural+effusion

Leading Causes of Pleural Effusion in the United States

Approximately 1.5 million pleural effusions are diagnosed in the United States each year

Leading Causes of Pleural Effusion in the US (according to analysis of patients subjected to thoracentesis)			
Cause	**Annual Incidence**	**Transudate Effusion**	**Exudate Effusion**
Congestive heart failure	500,000	Yes	No
Pneumonia	300,000	No	Yes
Cancer	200,000	No	Yes
PE	150,000	Sometimes	Sometimes
Viral disease	100,000	No	Yes
CABG	60,000	No	Yes
Cirrhosis with ascites	50,000	Yes	No

N ENGL J MED 2002; 346:1971-1977

Patient History and Physical Examination is the First Step in Evaluation of Pleural Effusion

The history and physical examination are critical in guiding the evaluation of pleural effusion

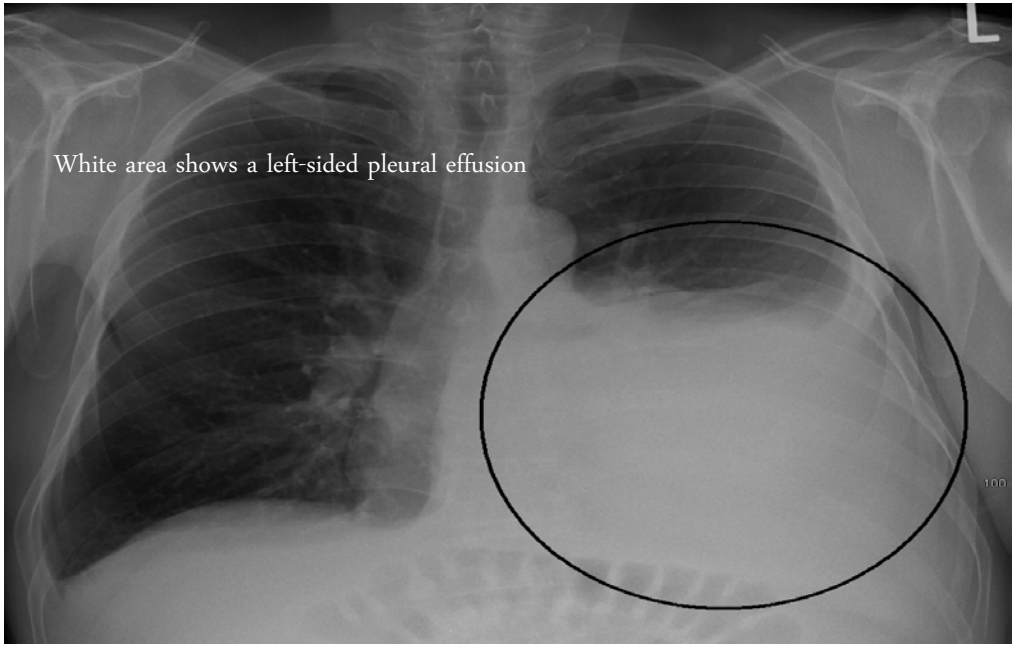
Signs and symptoms of an effusion vary depending on the underlying disease, but dyspnea, cough, and pleuritic chest pain are common.

Respiration. 2008;75(1):4-13.

Imaging Modalities Aid in the Evaluation of Pleural Effusion

Imaging modalities include:

- X-ray
- CT Scan
- Ultrasound

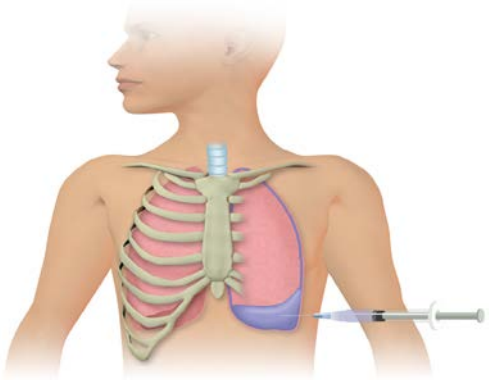


James Heilman, MD. Author GNU Free Documentation License

Pleural Effusion Diagnosis

When a pleural effusion is discovered, two questions need to be answered:

1. Is the effusion a transudate (is it due to systemic factors) or is it an exudate (is it due to disease of the pleura itself)?
2. If the effusion is an exudate, what is the disease responsible for its production?



Thoracentesis is a procedure to remove fluid from the pleural space for analysis:

- Protein to serum ratio
- Pleural fluid lactate dehydrogenase (LDH) to serum LDH
- **pH**
- Glucose
- Amylase

Light's Criteria:
Distinguish Transudate from Exudate Pleural Effusion

Light's criteria is the benchmark in classifying pleural fluid :

- Ratio of pleural fluid protein to serum protein greater than 0.5
- Ratio of pleural fluid lactate dehydrogenase (LDH) to serum LDH greater than 0.6
- Pleural fluid LDH greater than two thirds the upper limit of normal for serum LDH

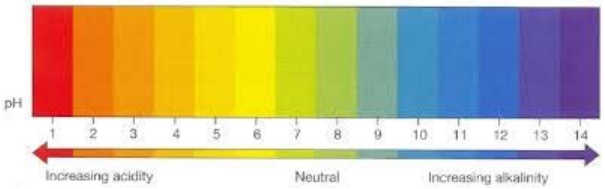
  (a cutoff value of 200 IU/L was used previously)

Exudate pleural effusion if it meets *any one* of the criteria above.

If all three characteristics are not met, then the fluid is classified as a transudate.

http://www.nlm.nih.gov/medlineplus/ency/article/000086.htm

The Value of pH Analysis on Pleural Fluid



- **Pleural fluid pH in a normal, healthy adult is ~7.60-7.66, with typical value of 7.64**
  - Slightly alkaline when compared with blood pH (7.35-7.45)
  - The relatively high bicarbonate concentration of pleural fluid accounts for this difference in pH
- **The pH of pleural effusions is lower than that of normal pleural fluid**
- **Transudative effusions generally having a higher pH - 7.45-7.55 - than exudative effusions**
- **Exudative effusions generally have a pH in the approximate range of 7.30-7.45, with some important exceptions**

Fam Physician 2006; 73: 1211-20, Lung 1979; 156: 63-69, Am J Physiology 1973; 224: 857-61

The Value of pH Analysis on Pleural Fluid

- **All transudative and most exudative effusions have a pH >7.30**
- **Pleural fluid pH <7.30 (termed pleural acidosis) is associated with a limited number of conditions:**
  - **Pneumonia**
  - **Malignant disease**
  - **Tuberculosis**
  - **Rheumatoid disease**
  - **Esophageal rupture** - lowest pleural fluid pH (5.0-6.5)
    - A review of 475 patients with pleural effusion revealed 59 patients with pleural fluid pH <6.0
    - In all 59 cases the cause of the pleural effusion was esophageal rupture
    - Pleural fluid pH of <6.0 virtually diagnostic of esophageal rupture

Chest 1974; 66: 454-56

The Value of pH Analysis on Pleural Fluid – Transudative Effusion

- **Higher pleural fluid pH is seen in transudative effusions resulting from congestive heart failure**
  - Light et al measured pleural fluid pH in 178 patients, including 39 with heart failure.
  - In all but four of these 39 patients, pleural fluid pH was >7.4 and ranged from 7.40 to 7.58 (median 7.49).
  - The four patients with pleural fluid pH <7.4 had an accompanying metabolic or respiratory acidosis, highlighting the fact that acidemia can itself cause a lowering of pleural fluid pH, which may complicate the interpretation of pleural fluid pH results.

Chest 1973; 64: 591-96

The Value of pH Analysis on Pleural Fluid – Transudative Effusion

- **Transudative fluid results from imbalances in hydrostatic and oncotic forces and are caused by a limited number of recognized clinical conditions such as heart failure and cirrhosis**
- **Less common causes include:**
  - Nephrotic syndrome
  - Atelectasis
  - Peritoneal dialysis
  - Constrictive pericarditis
  - Superior vena caval obstruction
  - Urinothorax
- **Transudative effusions usually respond to treatment of the underlying condition:**
  - Interesting, 25% of pleural effusions are resolved within 48 hours with aggressive diuretic therapy

Chest. Apr 1997;111(4):970-80 and *Chest*. Sep 2009;136(3):656-8

The Value of pH Analysis on Pleural Fluid - Parapneumonic Effusion

- **Pneumonia is the second most common cause of pleural effusion after congestive heart failure**
- **Parapneumonic effusions (PPE) - approximately 20-40 % of patients hospitalized with pneumonia develop an exudative pleural effusion. PPE also arise from lung abscess, or bronchiectasis**

Uncomplicated	Complicated	Empyema
• pH is >7.3 (7.33-7.47) • Generally respond well to antibiotic treatment	▪ Loculated pH is 6.70- 7.21 ▪ Presence of pus, gram stain-positive pleural fluid or pH <7.0 ▪ Treatment includes chest tube drainage (tube thoracostomy) and antibiotics	▪ Collection of pus in existing anatomical cavity, i.e. lung pleura ▪ pH 6.29-7.28 ▪ Treatment includes antibiotics, drainage, re-expansion of lung, decortication

- **pH of 7.2 as a cut-off value** is based on a large meta-analysis study of pleural fluid pH in PPE
- Study demonstrated **pleural fluid pH** better able to **predict the need for tube drainage** than either pleural fluid LDH activity or glucose

Proc Am Thorac Soc 2006; 375-80

The Value of pH Analysis on Pleural Fluid - Parapneumonic Effusion

- A low pleural fluid pH value has prognostic and therapeutic implications for patients with parapneumonic and malignant pleural effusions
- A pH value <7.20 in a patient with a parapneumonic effusion indicates the need for urgent drainage of the effusion, while a pleural fluid pH of >7.30 suggests that the effusion may be managed with systemic antibiotics alone
- In malignant effusions, a pleural fluid pH of <7.3 has been associated in some reports with more extensive pleural involvement, higher yield on cytology, decreased success of chemical pleurodesis, and shorter survival times.

Ann Intern Med. Oct 1972;77(4):507-13

Pleural Fluid Analysis

- Pleural fluid pH is frequently not measured correctly
  - 32% correctly use a Blood Gas machine
  - 56% use a dip stick or pH indicator paper
  - 12% use a pH meter
- In the American College of Chest Physicians (ACCP) consensus statement on the treatment of parapneumonic effusions, pH is the preferred pleural fluid chemistry test (determined using a blood gas analyzer) for classifying the category of a parapneumonic effusion for subsequent management.
- Studies have shown that results from pH meters and pH sticks can be significantly inaccurate.

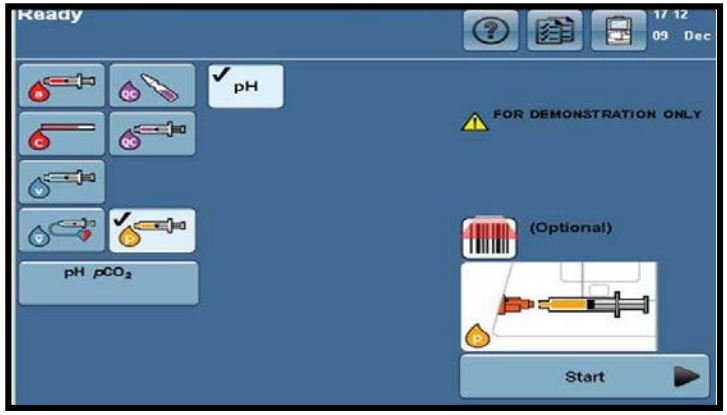
Proper Sample Handling for Pleural Fluid pH Testing

- Pleural fluid should be collected *anaerobically* into a heparinized blood gas syringe
  - Collecting pleural fluid into heparinized syringes helps prevent clot formation
- Expel all air from the syringe to eliminate any room air contamination
- Care should be taken to not contaminate the sample with even a trace of local anesthetic (lidocaine) used to prepare the patient for thoracentesis
- Analyze samples on a blood gas system within 1 hour of collection
- Reluctance to use blood gas analyzers is attributed in part to the fear that pleural fluids may block or damage electrodes
- Note: There are no clearly defined standard methods for the collection of pleural fluid for pH measurement

Am J Respir Crit Care Med 2008; 178: 483-90

Pleural Fluid Analysis

RAPIDPoint® 500 Blood Gas System



- ✓ FDA validated
- ✓ When enabled, only pH will be displayed
- ✓ No additional steps required

Take Home Messages for Pleural Fluid pH Analysis

- **Pleural effusion, excess fluid in the pleural space, has many possible causes, the most common are:**
  - Congestive heart failure
  - Pneumonia
  - Malignant disease
- **Pleural effusions are classified as either transudates or exudates**
- **Normal pleural fluid has a pH of 7.60-7.66 ; pH of pleural effusions is almost invariably <7.5**
- **pH of transudates generally higher (7.45-7.55) than exudates (7.30-7.40)**
- **Pleural fluid acidosis (pH <7.3) occurs when pleural effusion results from:**
  - esophageal rupture
  - tuberculosis
  - rheumatoid disease
  - malignant disease (in most cases pH >7.3)
  - pneumonia (in most cases pH >7.3)

Take Home Messages for Pleural Fluid pH Analysis

- The most important clinical utility of pleural fluid pH measurement is assessment of patients with parapneumonic and malignant pleural effusions
- In patents with parapneumonic effusion, pleural fluid pH <7.2 indicates advanced disease and need for urgent tube drainage in addition to antibiotic therapy
- In patients with parapneumonic effusion, pleural fluid pH >7.2 indicates that antibiotic therapy alone is probably sufficient therapy
- In patients with malignant effusion, pleural fluid pH <7.3 indicates reduced survival and is a contraindication for pleurodesis
- Blood gas analyzers should be used to measure pleural fluid pH - pH indicator sticks and pH meters are not suitable
- Pleural fluid for pH measurement should be collected anaerobically in a heparinized syringe and analyzed within 1 hour of collection

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