

### **Objectives :**

- ★ Describe the pathophysiology of a pleural effusion.
- ★ Describe the main causes of a pleural effusion.
- ★ Differentiate among the manifestations of fluid collections.
- ★ Describe the signs and symptoms of a pleural effusion
- ★ Explain diagnostic methods.
- ★ Describe the various treatment options.

#### **Color index**

Original text Females slides Males slides Doctor's notes <sup>438</sup> Doctor's notes <sup>439</sup> Text book Important Golden notes Extra

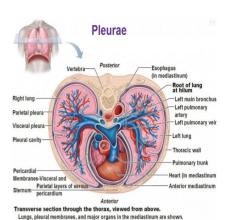
# **Pleural Effusion**

### Pleura<sup>1</sup>

- Serous fluid (5-15ml) that allows for the parietal pleura (outer lining) and visceral pleura (inner lining) to glide over each other without separation
- Pleural fluid is produced by the parietal pleura and absorbed by the visceral pleura as a continuous process.
- The visceral pleura absorbs fluid, which then drains into the lymphatic system and returns to the blood
- about 100-200 ml of fluid circulates through the pleural space within a 24-hour period.

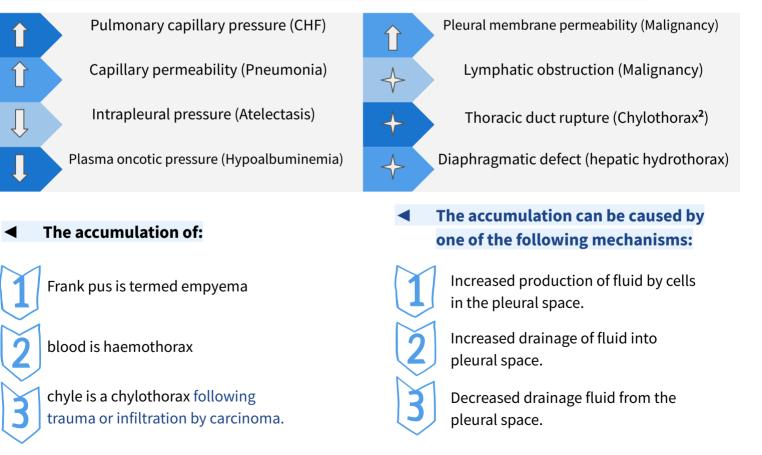
## Pleural effusion

- **Pleural effusion** is an excessive accumulation of **serous fluid** within the **pleural space**.
- Is there a normal effusion ? NO.. there is only normal pleural FLUID.
- Fluid accumulate at lower margins



The thorax, lungs and pleural Pleural space Parietal pleura pleura Parietal Pleural space Robe Componential Robe Robe

## Development of Pleural effusion The doctor said it's not imp



functions of pleural fluid : facilitate pleural movement and lubricate (to prevent atelectasis)
 Caused by accumulation of lymph in the pleural space. Fluid analysis is cloudy, milky fluid with high concentrations of lipids (triglycerides, cholesterol, <u>chylo</u>microns, and fat-soluble vitamins) remember <u>chylo</u>thorax analysis reveals <u>chylo</u>microns and other fat components

# 2



# **Causes and types of pleural effusion**

Causes	<ol> <li>CHF is the most common cause</li> <li>Pneumonia (bacterial)</li> <li>Malignancies:         <ul> <li>lung (36%)</li> <li>breast (25%),</li> <li>lymphoma (10%)</li> </ul> </li> </ol>	<ol> <li>Pulmonary embolism (PE)</li> <li>Viral diseases</li> <li>Cirrhosis with ascites (also known as hepatic hydrothorax)</li> </ol>
	Transdative <sup>1</sup>	Exudative <sup>1</sup>
Pathophysiology	Transudate THydrostatic pressure and/or J.Oncotic pressure	Fluid, protein, cell leakage
	• Due to elevated capillary hydrostatic	<ul> <li>↓ lymphatic flow from pleural surface due to damage to pleural membranes or vasculature.</li> </ul>
	pressure in visceral or parietal pleura	<ul> <li></li></ul>
	<ul> <li>(e.g., CHF)</li> <li>Due to decreased plasma oncotic pressure (e.g., hypoalbuminemia)</li> <li>Due to decreased intrapleural pressure (eg. atelectasis)</li> <li>The protein content is less than 30 g/L, the LDH is less than 200 IU/L and the fluid to serum LDH ratio is below 0.6.</li> </ul>	<ul> <li>Thoracic Duct rupture (eg. Chylothorax)<sup>4</sup></li> <li>Lymphatic Obstruction (eg. malignancy)<sup>4</sup></li> <li>↑ capillary permeability (eg. Pneumonia)<sup>4</sup></li> <li>The protein content is over 30 g/L and the LDH is more than 200 IU/L.</li> <li>→ If an exudative effusion is suspected, perform the following tests on the pleural fluid: differential cell count, total protein, LDH, glucose, pH, amylase, triglycerides, microbiology, and cytology.</li> </ul>
Main causes	<ul> <li>the causes are always related to a big organ</li> <li>CHF there is a trick with HF, the patient on long furosemide treatment will give exudate pleural effusion</li> <li>Nephrotic syndrome</li> <li>Hypoalbuminemia</li> <li>Hepatic hydrothorax (Liver Cirrhosis)</li> <li>Atelectasis</li> <li>Hypothyroidism</li> </ul>	<ol> <li>Tuberculosis</li> <li>Pneumonia + empyema</li> <li>Malignancy <sup>2-3</sup> (rarely transudate)</li> <li>PE <sup>5</sup></li> <li>Inflammatory:         <ul> <li>a. pancreatitis, ARDS, uremic pleurisy, etc</li> <li>Connective tissue disease.</li> <li>autoimmune rheumatic diseases (SLE, rheumatoid arthritis and sjogren's syndrome)</li> <li>Viral/parasitic disease</li> <li>Esophageal rupture</li> <li>Post coronary bypass surgery</li> <li>Post myocardial syndrome</li> <li>Drug induced</li> </ul> </li> </ol>

1-according to the Dr the red ones are the main ones and it's a common question in the exam.

- 2- In females, what's the most common non-lung malignancy that will cause pleural effusion ? Breast cancer.
- 3- In males, what's the most non-lung malignancy that will cause pleural effusion ? Adrenal cancer.
- 4- it was mentioned in the previous page not extra
- 5- it's mixture of transudate and exudate, but exudate is more prominent

### **Pleural fluid pearls:**

- Elevated pleural fluid amylase 1.
- Milky, opalescent fluid 2.
- 3. Frankly purulent fluid
- **Bloody Effusion** 4.
- Exudative effusions that are primarily 5. lymphocytic
- pH < 7.2 (most important indication for 6. inserting chest drain)

Light's criteria:

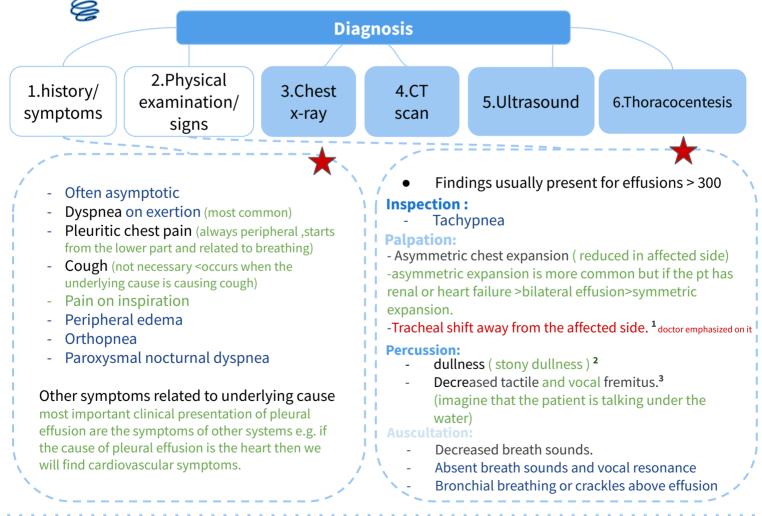
- Esophageal rupture, pancreatitis, 1. malignancy.
- 2. Chylothorax (lymph in the pleural space) 3.
  - Empyema (pus in the pleural space)
- 4. Malignancy

5. ΤB

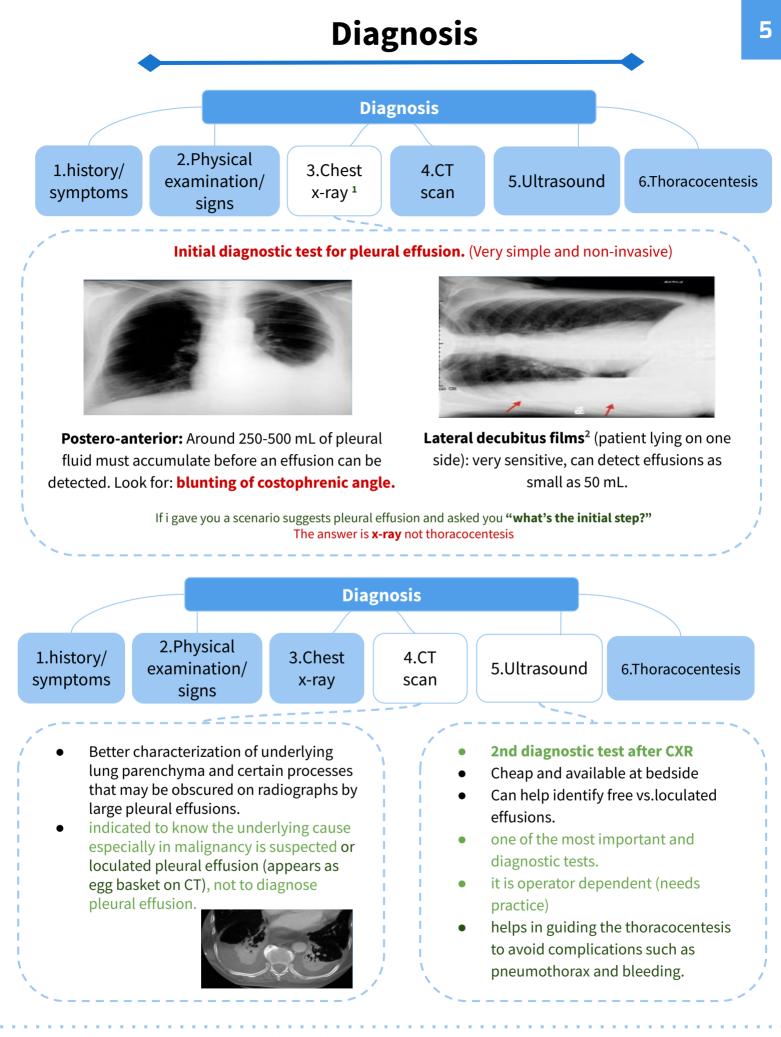
Parapneumonic effusion or empyema 6.

We may ask you as a scenario, and the criteria in a schedule in indirect way

- 98% sensitive and 83% specific for exudative effusion using Light's criteria.
- Pleural effusion is exudative if one or more of the following:
  - 1. Ratio of pleural fluid protein level to serum protein level > 0.5
  - 2. Ratio of pleural fluid LDH level to serum LDH level > 0.6
  - 3. Pleural fluid LDH level > 2/3 the upper limit of normal for serum LDH level.
- absence of all 3 criteria = Transudative

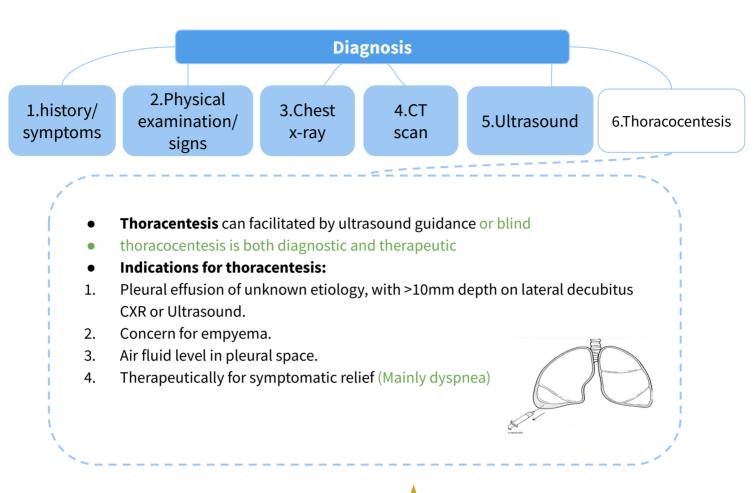


1- trachea is normally central and slightly to the right, in case of pleural effusion or pneumothorax it will shift to the other side, in case of mass it will shift to the same side. Anything that increases pressure or volume in one hemithorax will push the trachea and mediastinum away from that side. Any disease which causes volume loss in one hemithorax will pull the trachea over towards that side. The trachea may be pulled towards areas of fibrosis or collapse. It may be **pushed away** by masses, a goitre, lymphadenopathy large pleural effusion or a tension pneumothorax 2- Normally  $\rightarrow$  resonant, Pneumothorax  $\rightarrow$  hyperresonant, Pleural effusion  $\rightarrow$  stony dullness 3-increase in consolidation and mass



1- it should be done for any patient suspected to have pleural effusion 2-nowadays not clinically significant

# Diagnosis



# Comparison from the Dr:

- complicated and uncomplicated parapneumonic effusion> look at the chemistry
- Empyema and complicated parapneumonic effusion > look at the color

	Туре			
Character	Empyema	Complicated Parapneumonic effusion <sup>1</sup>	Uncomplicated parapneumonic effusion	
Color	Pus Tur		bid	
рН²	< 7.2		normal	
Glucose <sup>2</sup>	Very low (≤ 60 mg/dL) Chest tube + Antibiotics		Low	
Treatment			Antibiotics	

1- if we don't treat them as empyema they will develop empyema

2- PH and glucose low and the predominant cells lymphocytes? Malignancy

# **Pleural fluid evaluation**

# **5Cs:**

#### fin Color:

#### **Doctor's notes:**

- **Yellow:** Any of the mentioned causes below can cause yellow it's the most common color (also called urine color)
- Pus (thick & not milky): empyema
- White/Milky: Lymphatic obstruction<sup>1</sup>
- **Red:** bleeding (could be due to trauma or iatrogenic while performing thoracentesis), malignancy, TB, connective tissue disease.
- If a countanour of bloody pleural effusion was brought to you and you were asked if it was caused by a blunt trauma or caused iatrogenically .. how would you know ? pleural fluid with hematocrit greater than 50% of the patient's blood then it's blunt trauma.
- Black/Brown: fungal infection
- **Turbid (cloudy):** Acute bacterial infection (Parapneumonic effusion)
- **Green:** Fungal infection. Rarely seen.
- **Blue:** can be found in the pleural space after instillation of methylene blue into the pleural space to localize a bronchopleural fistula

### Cytology:

• To tell you if there's malignancy or not e.g. cells of metastatic adenoma from the breast.

### **Culture:**

• for diagnosis of Parapneumonic effusion, Empyema, TB<sup>2</sup>. If patient was in septic shock it may be positive for klebsiella pneumonia

### Cell count:

- It's simply a CBC of that fluid.. Don't know any specific details just look for the DDx depending on the **predominant cells (>60%)** not the total number of WBC
- **Lymphocytic(>50%) :** Malignancy (30-35%) , TB (15-20%) , Sarcoidosis. Indicates usually chronic infection and accompanies red colored effusion
- PMN: Empyema, Parapneumonic, Rheumatoid, Pulmonary infarction. Indicates usually acute infection and accompanies yellow turbid colored effusion
- **PMNs or Lymphocytic:** PE, Conn tissue disease, Post-cardiac injury.
- Eosinophilic (> 10%) :Trauma, pneumothorax, Malignancy, Asbestos, parasites, pneumonia.
- **RBC > 100,000/mm:** Malignancy, Trauma, Pulmonary infarction.

### **Chemistry:**

- pH: decrease in acute infection, empyema, malignancies, TB, connective tissue diseases and sometimes esophageal rupture
- Glucose: decrease in malignancy ,acute infection (parapneumonic effusion) and connective tissue disease

1- usually associated with malignancies especially breast cancer and thoracic duct injury

2- TB culture rarely become positive, so we need another diagnostic test for TB, pleural biopsy



#### • pleural TB is diagnosed by pleural biopsy

#### Routine Pleural Fluid Tests for Pleural Effusion

	Test	Test value	Suggested diagnosis	Comments
Supportive but not diagnostic	Adenosine deaminase (ADA)	>40 U per L (667 nkat per L)	Tuberculosis (>90 percent), empyema (60 percent), complicated parapneumonic effusion (30 percent), malignancy (5 percent), rheumatoid arthritis <sup>5</sup>	In the United States, ADA is not routinely requested because of the low prevalence of tuberculous pleurisy.
	Cytology	Present	Malignancy	Actively dividing mesothelial cells can mimic an adenocarcinoma.
	Glucose	<60 mg per dL (3.3 mmol per L)	Complicated parapneumonic effusion or empyema, tuberculosis (20 percent), malignancy (<10 percent), rheumatoid arthritis <sup>5</sup>	In general, pleural fluids with a low glucose level also have low pH and high LDH levels.
	Lactate dehydrogenase (LDH)	>Two thirds of upper limits of normal for serum LDH	Any condition causing an exudate	Very high levels of pleural fluid LDH (> 1,000 U per L) typically are found in patients with complicated parapneumonic pleural effusion and in about 40 percent of those with tuberculous pleurisy. <sup>5</sup>
	LDH fluid to serum ratio	>0.6	Any condition causing an exudate	Most patients who meet the criteria for an exudative effusion with LDH but not with protein levels have either parapneumonic effusions or malignancy. <sup>3</sup>
	Protein fluid to serum ratio	>0.5	Any condition causing an exudate	A pleural fluid protein level >3 mg per dL suggests an exudate, but when taken alone this parameter misclassifies more than 10 percent of exudates

#### **Optional Pleural Fluid Tests for Pleural Effusion**

Test	Test value	Suggested diagnosis	Comments
Amylase	> Upper limit of normal	Malignancy (<20 percent), pancreatic disease, esophageal rupture <sup>5,16</sup>	Obtain when esophageal rupture or pancreatic disease is suspected. The amylase in malignancy and esophageal rupture is of the salivary type.
Cholesterol	>45 to 60 mg per dL (1.16 to 1.55 mmol per L)	Any condition causing an exudate	Measure if chylothorax or pseudochylothorax is suspected. This parameter taken alone misclassifies 10 percent of exudates and 20 percent of transudates. <sup>13</sup>
Culture	Positive	Infection	Obtain in all parapneumonic pleural effusions because a positive Gram stain or culture should lead to prompt chest tube drainage. <sup>14,15</sup>
Hematocrit fluid to blood ratio	≥0.5	Hemothorax	Obtain when pleural fluid is bloody. Hemothorax most often originates from blunt or penetrating chest trauma.
Interferon*	Different cutoff points	Tuberculosis <sup>17</sup>	Consider when ADA is unavailable or nondiagnostic and tuberculosis is suspected.
NT-proBNP	>1,500 pg per mL	Heart failure <sup>18</sup>	If available, consider testing when heart failure is suspected and exudate criteria are met. <sup>19</sup>
рН	<7.20	Complicated parapneumonic effusion or empyema, malignancy (< 10 percent), tuberculosis (< 10 percent), esophageal rupture <sup>5</sup>	Obtain in all nonpurulent effusions if infection is suspected A low pleural fluid pH indicates the need for tube drainage only for parapneumonic pleural effusions.
Polymerase chain reaction†	Positive	Infection <sup>20,21</sup>	Consider when infection is suspected. Sensitivity of polymerase chain reaction to detect <i>Mycobacterium tuberculosis</i> in pleural fluid varies from 40 to 80 percent and is lower in patients with negative mycobacterial cultures.
Triglycerides	>110 mg per dL (1.24 mmol per L)	Chylothorax	Obtain when pleural fluid is cloudy or milky. Chylothorax is caused by lymphoma or trauma. Not all chylous pleural effusions appear milky white or whitish.
Tumor markers‡	Different cutoff points	Malignancy	Consider when malignancy is suspected and thoracoscopy is being considered. Except for telomerase activity, <sup>22</sup> individual tests tend to have low sensitivity (< 30 percent) when looking for the utmost specificity. <sup>23,24</sup>

# Treatment



# Treat underlying disease

- Treatment of pleural effusion = treatment of the cause
- **thoracentesis** : is done for symptomatic relief or to take a sample from pleural fluid and removed immediately
- **chest tube:** can remain connected to the pt up to 4 days

#### **Parapneumonic effusions**

 Uncomplicated: antibiotics alone.
 Complicated or empyema:

#### MCQ

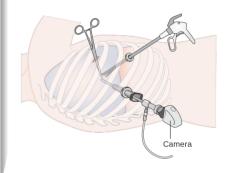
- Chest tube drainage and antibiotics.
- Intrapleural injection of thrombolytic agents (streptokinase or urokinase); may accelerate the drainage.
- Surgical lysis of adhesions may be required.

**Malignant effusion** 

- chest tube +/pleurodesis (sclerosants) VATS
- Malignant pleural effusions that reaccumulate and are symptomatic can be aspirated to dryness followed by the instillation of a sclerosing agent such as tetracycline or talc.

#### Hemithorax involved/empyema

 tube thoracostomy +/-VATS (video assisted thoracoscopic surgery)



#### **Transudative effusion**

- Diuretics and sodium restriction.
- Therapeutic thoracentesis (only if massive effusion is causing dyspnea)

#### **Exudative effusion**

• Treat underlying cause.

1-procedure in which a needle is inserted into the pleural space between the lungs and the chest wall. This procedure is done to remove excess fluid, known as a pleural effusion, from the pleural space to help you breathe easier.

# **Cases (Doctor's slides)**

### Case study 1:

A 55-year-old man presents with progressive shortness of breath. Other than a history of heavy smoker, the patient has no significant past medical history. Breath sounds are absent two-thirds of the way up on the left side of the chest. Percussion of the left chest reveals stony dullness, the trachea appears to be deviated toward the right.

· · · ·	Which of the following diagnoses is most likely?
А.	Bacterial pneumonia
В.	Viral pneumonia
С.	Bronchial obstruction
D.	Pleural effusion
Ε.	Pneumothorax
The co	prrect answer is D

### Case study 2:

A 67-year-old man presents to the emergency department with a 5-day history of fever and cough that produces green sputum. He has a history of tobacco use and ischemic cardiomyopathy with a left ventricular ejection fraction of 25%. He was admitted with a presumptive diagnosis of pneumonia and is started on antibiotics. A chest radiograph is obtained and shows a left-sided consolidation and moderate-size effusion.

Which of the following studies can be used to determine if the patient effusion is due to his CHF (a transudate) or is a parapneumonic effusion (an exudate)?
 A. Pleural fluid pH
 B. Pleural fluid glucose
 C. Pleural fluid cell count
 D. Lactate dehydrogenase (LDH)
 The correct answer is D

# **Cases (Doctor's slides)**

### Case study 3:

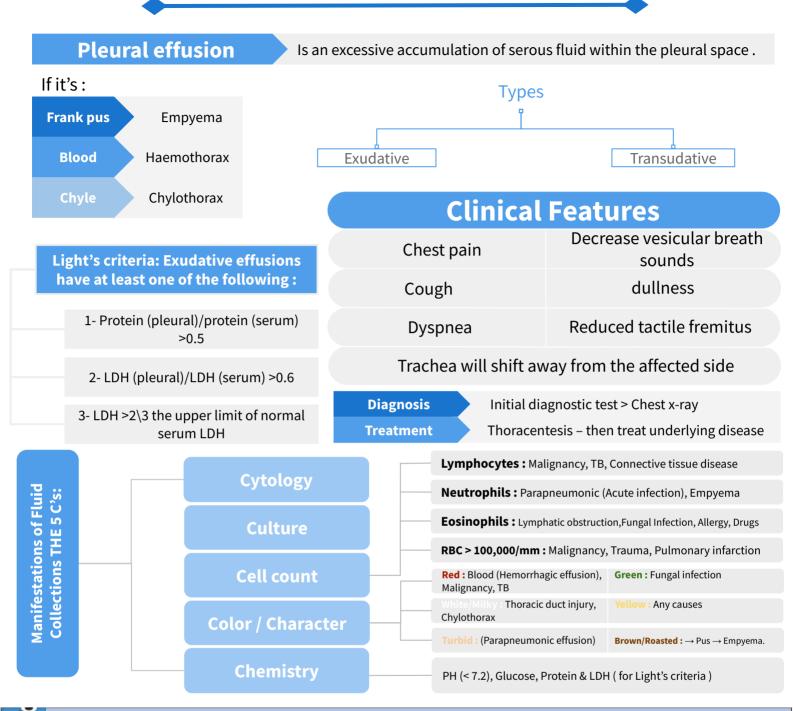
✤ A 59-year-old male presents with a community acquired pneumonia complicated by pleural effusion. A thoracentesis is performed, but the results are not currently available.

Which characteristic of the pleural fluid is most suggestive complicated parapneumonic pleural effusion?
 A. Presence of more than 30% polymorphonucleocytes (PMNs)
 B. Glucose less than 150 mg/dl
 C. Presence of more than 100 white blood cells
 D. pH less than 7.20
 E. Lactate dehydrogenase (LDH) more than two-thirds of the normal upper limit for serum
 The correct answer is D



- 70 year old gentleman brought to the hospital by his family after he developed right sided weakness, slurred speech, vomiting, cough and fever, physical examination revealed bronchial breathing, and chest X-Ray showed right lower lobe consolidation.
  - What is the most likely organism? anaerobes (klebsiella pneumonia) aspiration pneumonia
     Treatment? clindamycin
     after 14 days the patient had chest pain and shortness of breath, cxr showed pleural effusion. what is next step of management? Thoracocentesis
     Thoracocentesis was done and pus was coming out. what is the next step of management? chest tube drainage + antibiotic

# Summary



Cause	Appearance of fluid	Type of fluid	Predominant cells in fluid	Other diagnostic features
Tuberculosis	Serous, usually amber-coloured	Exudate	Lymphocytes (occasionally polymorphs)	Positive tuberculin test Isolation of <i>M. tuberculosis</i> from pleural fluid (20%) Positive pleural biopsy (80%) Raised adenosine deaminase
Malignant disease	Serous, often blood-stained	Exudate	Serosal cells and lymphocytes Often clumps of malignant cells	Positive pleural biopsy (40%) Evidence of malignancy elsewhere
Cardiac failure	Serous, straw-coloured	Transudate	Few serosal cells	Other signs of cardiac failure Response to diuretics
Pulmonary infarction	Serous or blood-stained	Exudate (rarely transudate)	Red blood cells Eosinophils	Evidence of pulmonary infarction Obvious source of embolism Factors predisposing to venous thrombosis
Rheumatoid disease	Serous Turbid if chronic	Exudate	Lymphocytes (occasionally polymorphs)	Rheumatoid arthritis: rheumatoid factor and anti-CCP antibodies Cholesterol in chronic effusion; very low glucose in pleural fluid
SLE	Serous	Exudate	Lymphocytes and serosal cells	Other signs of SLE Antinuclear factor or anti-DNA positive
Acute pancreatitis	Serous or blood-stained	Exudate	No cells predominate	Higher amylase in pleural fluid than in serum
Obstruction of thoracic duct	Milky	Chyle	None	Chylomicrons

(anti-CCP = anti-cyclic citrullinated peptide; SLE = systemic lupus erythematosus)

# **Lecture Quiz**

Q1: A 55-year-old man who has been smoking 20 cigarettes a day for the last 30 years has been diagnosed with a right-sided pleural effusion following admission with a week's history of shortness of breath. From the list below, select the most likely findings that one would ascertain during examination of the chest wall ?

A- Decreased air entry coupled increased vocal fremitus and resonant percussion on the right side of the chest

B- Normal air entry coupled decreased vocal fremitus and resonant percussion on the right side of the chest

C- Normal air entry coupled increased vocal fremitus and dull percussion on the right side of the chest D- Decreased air entry coupled decreased vocal fremitus and dull percussion on the side of the chest

Q2: A 54-year-old woman is seen in clinic with a history of weight loss, loss of appetite and shortness of breath. Her respiratory rate is 19 and oxygen saturations (on room air) range between 93 and 95 per cent. On examination, there is reduced air entry and dullness to percussion on the lower to mid zones of the right lung. There is also reduced chest expansion on the right. From the list below, select the most likely diagnosis ?

- A- Right middle lobe pneumonia
- B- Pulmonary embolism
- C- Right-sided pleural effusion
- D- Right-sided bronchial carcinoma

Q3: A 56-year-old woman who has recently been discharged from your ward, with oral antibiotics for right basal community-acquired pneumonia, is re-admitted with transient pyrexia and shortness of breath. She is found to have a right-sided pleural effusion which is drained and some pleural aspirate sent for analysis. The results reveal an empyema. Which of the following, from the pleural aspirate analysis, would typically be found in a patient with an empyema?

A- pH >7.2,  $\uparrow$  LDH,  $\uparrow$  glucose B- pH <7.2,  $\uparrow$  LDH,  $\uparrow$  glucose C- pH >7.2,  $\downarrow$  LDH,  $\downarrow$  glucose D- pH <7.2,  $\uparrow$  LDH,  $\downarrow$  glucose E- pH <7.2,  $\leftrightarrow$  LDH,  $\leftrightarrow$  glucose

Q4: Which one of the following is considered the most common cause of pleural effusion ?

A- Primary lung cancer B- Congestive heart failure C- Mesothelioma D- Trauma.

Q5: A 45-year-old woman with unexpected weight loss, loss of appetite and shortness of breath presents to you in clinic. On examination, there is reduced air entry and dullness to percussion in the right lung. A pleural tap is performed and the aspirate samples sent for analysis. You are told that the results reveal a protein content of >30 g/L. From the list below, select the most likely diagnosis:

- A- Bronchogenic carcinoma
- B- Congestive cardiac failure
- C- Liver cirrhosis
- D-Nephrotic syndrome
- E- Meig's syndrome

Answers: Q1:D | Q2:C | Q3:D | Q4:B | Q5:A

# GOOD LUCK !

