

**MINISTRY OF HEALTH CARE OF UKRAINE  
KHARKIV NATIONAL MEDICAL UNIVERSITY**

Department of Phthiology and Pulmonology

The 2nd Medical Faculty

**METHODICAL RECOMMENDATION  
FOR THE STUDENT'S SELF WORK**

Educative discipline

”Current Problems of Phthiology and Pulmonology”

for students of 5 course of 6<sup>th</sup> medical faculty

“Approved”

Educative-methodical counsel of  
Department of  
Phthiology and Pulmonology  
« \_\_\_\_ » \_\_\_\_\_ 20 \_\_\_\_ p.  
protocol № \_\_\_\_\_  
Head of Department  
Professor Shevchenko O.S.

KHARKIV – 2016

**Topic: Pleurisy and pleural effusion. Etiology, pathogenesis, path morphology, clinical picture, diagnostics, differential diagnosis, treatment.**

**1. Quantity of hours 4**

**2. Financial and methodical support of the topic:** tables, results of patients examination and their case histories, X-ray pictures.

**3. Currency of the topic.**

Pleural disease remains common, affecting over 3000 people per million population each year. It therefore presents a significant contribution to the workload of respiratory physicians. Pleural disease originates from a wide range of pathologies and a systematic approach to the investigation and management is therefore required.

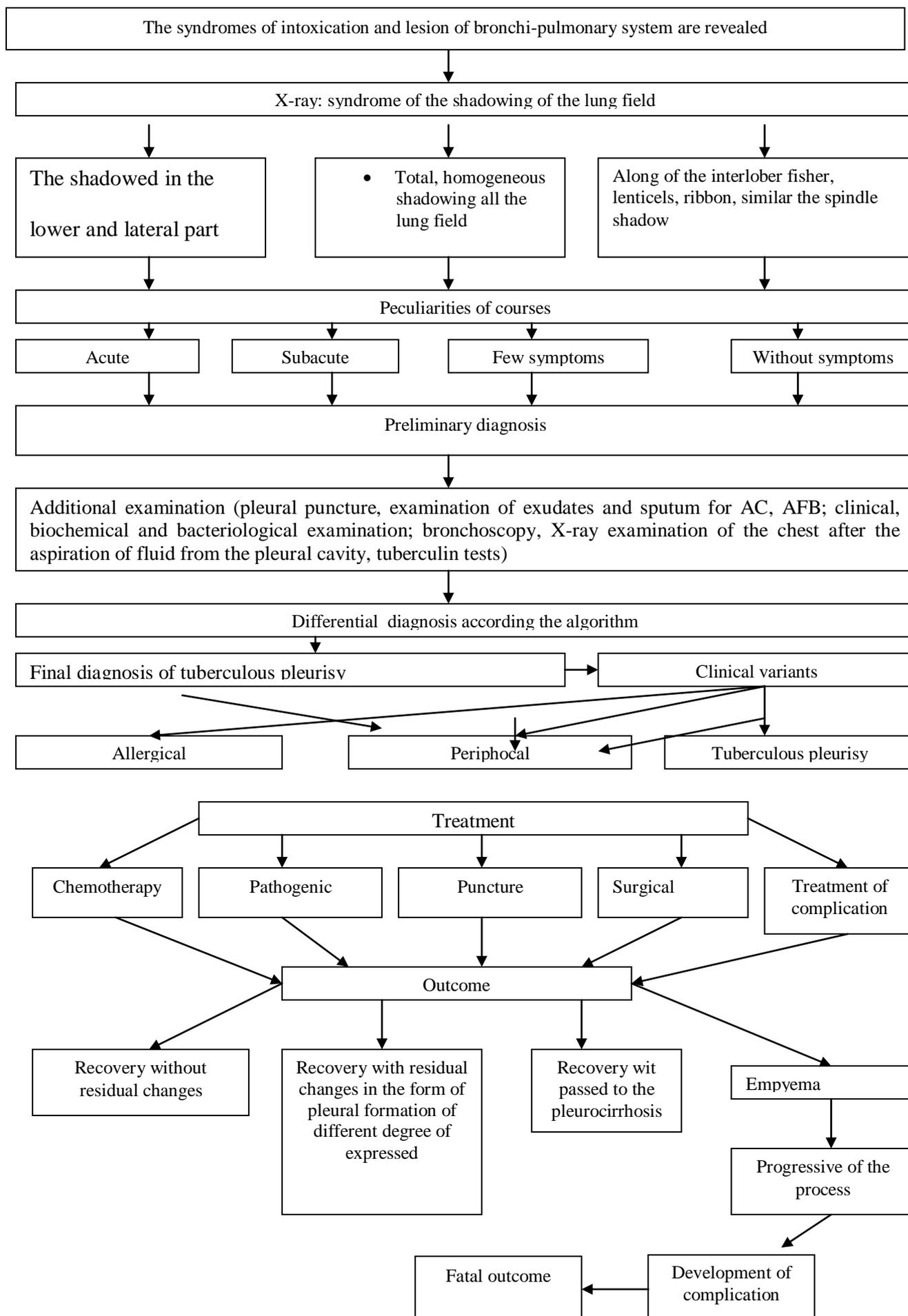
The evaluation of the patient with a pleural effusion requires a systematic history (including the duration of the effusion), physical examination, and pertinent laboratory tests to formulate a prethoracentesis diagnosis.

Over 40% of patients with community-acquired pneumonia develop an associated pleural effusion ('para-pneumonic' effusion) and about 15% of these become secondarily infected.

**4. Educational goal:**

- General mastering of the methods of examination of the patients with pleurisy; diagnosis and treatment of pleurisy
- a) **To know** definition of pleurisy and pleural effusion;
  - etiology and pathogenesis of pleurisy and pleural effusion;
  - classification of pleurisy and pleural effusion;
  - methods of investigations of pleurisy and pleural effusion.
- b) **To be able** to interpret data of laboratory and instrumental investigations in pleurisy and pleural effusion;
  - to manage a case with pleurisy and pleural effusion.
- c) To master **practical skills:**
  - Palpation of the chest (elasticity, resistance, vocal phremitus);
  - Topographic percussion of the lungs;
  - Assessment of low lung edge excursion;
  - Comparative percussion of lungs;
  - Auscultation of lungs;
  - Assessment of bronchophony;

## 5. Graphs of the logical structure



## 6. Reference student's card

### PLEURISY AND PLEURAL EFFUSION

**Basic Anatomy and Physiology** The pleura is the serous membrane that covers the lung parenchyma, the mediastinum, the diaphragm, and the rib cage. This structure is divided into the visceral pleura and the parietal pleura. The visceral pleura covers the lung parenchyma, not only at its points of contact with the chest wall, diaphragm, and mediastinum but also in the inter-lobar fissures. The parietal pleura lines the inside of the thoracic cavities. In accordance with the intrathoracic surfaces that it lines, it is subdivided into the costal, mediastinal, and diaphragmatic parietal pleura. The visceral and the parietal pleura meet at the lung root.

A pleural fluid is normally present between the parietal and the visceral pleura. This thin layer of fluid acts as a lubricant and allows the visceral pleura covering the lung to slide along the parietal pleura lining the thoracic cavity during respiratory movements. The space, or potential space, between the two layers of pleura is designated as the pleural space. The mediastinum completely separates the right pleural space from the left in humans. As previously mentioned, only a thin layer of fluid is normally present in this space (~10 ml in each pleural cavity), so it is a potential space rather than an actual one.

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Fluid that enters the pleural space can originate in the pleural capillaries, the interstitial spaces of the lung, the intrathoracic lymphatics, the intrathoracic blood vessels, or the peritoneal cavity. Pleural fluid contains protein at concentrations similar to the interstitial fluid, a small number of cells (predominantly mesothelium cells, macrophages and lymphocytes), and some large molecular weight proteins such as lactate dehydrogenase (LDH). Compared with serum, pleural fluid in

health also contains higher levels of bicarbonate, lower levels of sodium, and similar levels of glucose. These parameters change when disease processes affecting the adjacent lung or vascular tissue activate an immune response. Water and small molecules pass freely between mesothelium cells, while larger particles may be transported by cytoplasmic transport mechanisms or via the pleurolymphatic communication. The pleurolymphatic communication is poorly documented but probably consists of a series of stomas in selected areas of pleura overlying connective tissue and a series of dilated lymphatic channels with regulatory valves.

### **DEFINITION**

**Pleurisy** is an inflammation of the membrane that surrounds and protects the lungs (the pleura).

**Pleural effusion** is an abnormal collection of fluid in the potential space between the visceral and parietal pleura.

**Empyema** is an infection in the pleural space.

### **ETIOLOGY, PATHOLOGY AND PATHOPHYSIOLOGY**

#### **Approximate Annual Incidence of Various Types of Pleural Effusions**

Congestive heart failure	37%
Para pneumonic effusion	22%
Malignant pleural effusion (lung breast, lymphoma, other)	15%
Pulmonary embolization	11%
Viral disease	7%
Cirrhosis with ascites	4%
Others	4%

Pleural fluid accumulates when pleural fluid formation exceeds pleural fluid absorption. Normally, fluid enters the pleural space from the capillaries in the parietal pleura and is removed via the lymphatics situated in the parietal pleura.

Fluid can also enter the pleural space from the interstitial spaces of the lung via the visceral pleura or from the peritoneal cavity via small holes in the diaphragm. The lymphatics have the capacity to absorb 20 times more fluid than is normally formed. Accordingly, a pleural effusion may develop when there is excess pleural fluid formation (from the interstitial spaces of the lung, the parietal pleura, or the peritoneal cavity) or when there is decreased fluid removal by the lymphatics.

### **General Causes of Pleural Effusions**

#### *Increased pleural fluid formation*

##### 1. Increased interstitial fluid in the lung

Left ventricular failure, pneumonia, and pulmonary embolus

##### 2. Increased intravascular pressure in pleura

Right or left ventricular failure, superior vena caval syndrome

##### 3. Increased permeability of the capillaries in the pleura

Pleural inflammation

##### 4. Increased levels of vascular endothelial growth factor

##### 5. Increased pleural fluid protein level

##### 6. Decreased pleural pressure

Lung atelectasis or increased elastic recoil of the lung

##### 7. Increased fluid in peritoneal cavity

Ascites or peritoneal dialysis

##### 8. Disruption of the thoracic duct

##### 9. Disruption of blood vessels in the thorax

#### *Decreased pleural fluid absorption*

##### 1. Obstruction of the lymphatics draining the parietal pleura

##### 2. Elevation of systemic vascular pressures

##### 3. Superior vena caval syndrome or right ventricular failure

##### 4. Disruption of the aquaporin system in the pleura

Pleural effusions are categorized as transudates or exudates. Altered osmotic or hydrostatic forces cause transudative effusions. Notably, transudates contain low

protein. Exudative effusions develop from alterations in lymphatic drainage or abnormalities of the capillary permeability of the pleura itself. These effusions contain higher levels of protein. *TRANSUDATIVE PLEURAL EFFUSIONS*

1. Congestive heart failure (common cause)
2. Liver cirrhosis (common cause)
3. Pulmonary embolization
4. Nephrotic syndrome
5. Peritoneal dialysis (common cause)
6. Superior vena cava obstruction
7. Myxedema
8. Urinothorax

*EXUDATIVE PLEURAL EFFUSIONS*

1. Neoplastic diseases (common cause)
  - a. Metastatic disease
  - b. Mesothelioma
2. Infectious diseases (common cause)
  - a. Bacterial infections
  - b. Tuberculosis
  - c. Fungal infections
  - d. Viral infections
  - e. Parasitic infections
3. Pulmonary embolizm
4. Gastrointestinal disease
  - a. Esophageal perforation
  - b. Pancreatic disease
  - c. Intraabdominal abscesses
  - d. Diaphragmatic hernia
  - e. After abdominal surgery
  - f. Endoscopic variceal sclerotherapy
  - g. After liver transplant

5. Collagen-vascular diseases
  - a. Rheumatoid pleuritis
  - b. Systemic lupus erythematosus
  - c. Drug-induced lupus
  - d. Immunoblastic lymphadenopathy
  - e. Sjogren's syndrome
  - f. Wegener's granulomatosis
  - g. Churg-Strauss syndrome
6. Post-coronary artery bypass surgery
7. Asbestos exposure
8. Sarcoidosis
9. Uremia
10. Meigs' syndrome
11. Yellow nail syndrome
12. Drug-induced pleural disease
  - a. Nitrofurantoin
  - b. Bromocriptine
  - e. Procarbazine
  - f. Amiodarone
13. Trapped lung
14. Radiation therapy
15. Post-cardiac injury syndrome
16. Hemothorax
17. Iatrogenic injury
18. Ovarian hyper stimulation syndrome
19. Pericardial disease
20. Chylothorax

**COMPLAINTS, SYMPTOMS, SIGNS OF PLEURISY AND PLEURAL EFFUSION.**

- Cough (nonspecific)
- Chills (for pleurisy)
- Shortness of breath (for pleural effusion)
- Fever (for pleurisy)
- Weight loss (nonspecific)
- Poor appetite (nonspecific)
- Sharp chest pain with breathing. Pain can limit the movement on the side of the chest with pleurisy.
- Rapid shallow breaths (for pleural effusion)
- Inability to take a deep breath (for pleurisy)
- Dizziness

Patients with small effusions are often asymptomatic. Common complaints with symptomatic effusions are dyspnea, pleuritic chest pain, or cough. Patients may also have complaints related to their underlying disease or give a history of cancer, heart failure, or other comorbidity. The symptoms of a patient with a pleural effusion are mainly dictated by the underlying process causing the effusion. Many patients have no symptoms referable to the effusion. When symptoms are related to the effusion, they arise either from inflammation of the pleura, from compromise of pulmonary mechanics, from interference with gas exchange, or on rare occasions, from decreased cardiac output. A pleural effusion associated with pleuritic ***chest pain*** indicates inflammation of the pleura, specifically, the parietal pleura as the visceral pleura does not have pain fibers. Some patients with pleural effusions experience a dull, aching chest pain rather than pleuritic chest pain. This symptom is very suggestive that the patient has pleural malignancy. The presence of either pleuritic chest pain or dull, aching chest pain indicates that the parietal pleura is probably involved and that the patient has an exudative pleural effusion.

Ordinarily, the pain associated with pleural disease is well localized and coincides with the affected area of the pleura, because the parietal pleura is innervated mostly by the intercostal nerves. At times, however, pleuritic pain is referred to the abdomen because intercostal nerves are also distributed to the

abdomen. A notable exception to the localization of the pain occurs when the central portion of the diaphragmatic pleura is involved. The nerve supply to this portion of the parietal pleura is the phrenic nerve; therefore, inflammation of the central portion of the diaphragm is referred to the tip of the ipsilateral shoulder. Pleuritic pain felt simultaneously in the lower chest and ipsilateral shoulder is pathognomonic of diaphragmatic involvement.

A second symptom of pleural effusion is a dry, **nonproductive cough**. The mechanism producing the cough is not clear, although it may be related to pleural inflammation. Alternately, lung compression by the fluid may bring opposing bronchial walls into contact, stimulating the cough reflex.

The third symptom of pleural effusion is **dyspnea**. A pleural effusion acts as a space-occupying process in the thoracic cavity and therefore reduces all subdivisions of lung volumes. Small-to-moderate-sized pleural effusions displace rather than compress the lung and have little effect on pulmonary function. Larger pleural effusions obviously cause a significant reduction in lung volumes, but the improvement in pulmonary function following therapeutic thoracentesis is much less than what one would anticipate. The degree of dyspnea is frequently out of proportion to the size of the pleural effusion. Often, this feature is the result of compromised diaphragmatic function due to the weight of fluid on the diaphragm. At times, the diaphragm becomes inverted and this usually results in disproportionate dyspnea. Either pleuritic chest pain, with the resultant splinting, or concomitant parenchymal disease can also be responsible for the disproportionate dyspnea. When the pleural effusion is large, ventricular filling may be impeded, leading to decreased cardiac output and dyspnea. Arterial blood gases usually remain at clinically acceptable levels whatever the size of the effusion because of the reflex reduction in perfusion to the lung underlying the effusion.

## **PHYSICAL FINDINGS**

### **Inspection.**

When the chest of a patient with, or who is suspected of having, a pleural effusion is examined, particular attention should be paid to the relative sizes of the

hemithoraces and the intercostal spaces. If the pleural pressure is increased on the side of the effusion, that hemithorax will be larger, and the usual concavity of the intercostal spaces will be blunted or even convex.

Of course, in many patients with pleural effusions, the hemithoraces are equal in size and the intercostal spaces are normal.

**Palpation.** Palpation of the chest in patients with pleural effusions is useful in delineating the extent of the effusion. In areas of the chest where pleural fluid separates the lung from the chest wall, tactile fremitus is absent or attenuated because the fluid absorbs the vibrations emanating from the lung. Tactile fremitus is much more reliable than percussion for identifying both the upper border of the pleural fluid and the proper site to attempt a thoracentesis. With a thin rim of fluid, the percussion note may still be resonant, but the tactile fremitus is diminished. Palpation may also reveal that the cardiac point of maximum impulse is shifted to one side or the other. With large left pleural effusions, the cardiac point of maximum impulse may not be palpable. In patients with pleural effusions, the position of the trachea should always be ascertained because it indicates the relationship between the pleural pressures in the two hemithoraces. **Percussion.**

The percussion note over a pleural effusion is dull or flat. The dullness is maximum at the lung bases where the thickness of the fluid is the greatest. As mentioned earlier, however, the percussion note may not be duller if only a thin rim of fluid is present. Light percussion is better than heavy percussion for identifying small amounts of pleural fluid. If the dullness to percussion shifts as the position of the patient is changed, one can be almost certain that free pleural fluid is present.

**Auscultation.** Auscultation over the pleural fluid characteristically reveals decreased or absent breath sounds. Near the superior border of the fluid, however, breath sounds may be accentuated and take on a bronchial characteristic. This phenomenon has been attributed to increased conductance of breath sounds through the partially atelectatic lung compressed by the fluid. This accentuation of breath sounds does not mean that an associated parenchymal infiltrate is present.

Auscultation may also reveal a pleural rub. Pleural rubs are characterized by coarse, creaking, leathery sounds most commonly heard during the latter part of inspiration and the early part of expiration, producing a to-and-fro pattern of sound. Pleural rubs, caused by the rubbing together of the roughened pleural surfaces during respiration, are often associated with local pain on breathing that subsides with breath-holding. Pleural rubs often appear as pleural effusions diminish in size, either spontaneously or as a result of treatment, because the pleural fluid is no longer present between the roughened pleural surfaces.

**Extrapulmonary physical findings.** It is important to realize that an elevated hemidiaphragm can produce all the classic physical findings associated with a pleural effusion. Obviously, the chest is not the only structure that should be examined when evaluating a patient with a pleural effusion; clues to the origin of the effusion are often present elsewhere. The effusion is probably due to congestive heart failure (CHF) if the patient has cardiomegaly, neck vein distension, or peripheral edema. Signs of joint disease or subcutaneous nodules suggest that the pleural effusion is due to rheumatoid disease or lupus erythematosus (LE). An enlarged, nontender nodular liver or the presence of hypertrophic osteoarthropathy suggests metastatic disease, as do breast masses or the absence of a breast. Abdominal tenderness suggests a subdiaphragmatic process, whereas tense ascites suggests cirrhosis and a hepa-tothorax. Lymphadenopathy suggests lymphoma, metastatic disease, or sarcoidosis.

### **Para pneumonic effusions and empyema**

Para pneumonic effusions and empyema are specific types of exudative pleural effusions due to infection adjacent to or in the pleural space, respectively. They are most frequently due to extension of infection from an underlying pneumonia. Hence, risk factors for empyema are similar to those for pneumonia. One of the most common causes of empyema is aspiration. Patients at the highest risk for aspiration include those with poor dentition, alcohol abuse, seizure disorder, and absent gag reflex (e.g., comatose patients, patients with altered mental status, and patients undergoing general anesthesia). The infections are usually polymicrobial

and include Bacteroides, Fusobacterium, and Peptostreptococcus species. One should always consider methicillin-resistant Staphylococcus aureus and Mycobacterium tuberculosis as potential pathogens in any pulmonary infection. Another common cause of empyema is penetrating chest injury, which includes both trauma and iatrogenic injury. Empyema may be caused by contamination of the traumatic wound or inadequate skin preparation before medical procedures such as chest tube placement or thoracentesis.

**Instrumental investigations and laboratory tests Pleural aspiration** • A diagnostic pleural fluid sample should be gathered with a fine bore (21G) needle and a 50 ml syringe. The sample should be placed in both sterile vials and blood culture bottles and analyzed for protein, lactate dehydrogenase (LDH), pH, Gram stain, cytology, and microbiological culture.

### **Pleural fluid analysis**

- The appearance of the pleural fluid and any odour should be noted.
- A pleural fluid haematocrit is helpful in the diagnosis of haemothorax.
- The pleural protein should be measured to differentiate between a transudative and exudative pleural effusion. The classical way of separating a
  - The appearance of the pleural fluid and any odor should be noted.
- A pleural fluid haematocrit is helpful in the diagnosis of haemothorax.
- The pleural protein should be measured to differentiate between a transudative and exudative pleural effusion. The classical way of separating a transudate from an exudate is by pleural fluid protein, with exudates having a protein level of >30 g/l and transudates a protein level of <30 g/l. This will usually suffice if the patient's serum protein level is normal and pleural protein is less than 25 g/l or more than 35 g/l. If not, Light's criteria should be used (the pleural fluid is an exudate if one or more of the following criteria are met):
  1. pleural fluid protein/serum protein >0.5
  2. pleural fluid LDH/serum LDH >0.6
  3. pleural fluid LDH more than two-thirds normal upper limit for serum

A recent meta-analysis found that any *one* of the following findings can also be used to identify the fluid as an exudate:

1. Pleural fluid protein >2.9 g/dL
2. Pleural fluid cholesterol >45 mg/dL
3. Pleural fluid LDH >60% of the upper limit of normal serum LDH

An increased level of LDH in the fluid is nonspecific, but it is increased in pulmonary embolism, rheumatoid effusion, lymphoma, and most exudative effusions. The classification of pleural fluid into transudates and exudates does not permit the consideration of all causes. The most common cause of a transudate is congestive heart failure (pulmonary artery wedge pressure >25 mm Hg). The most common cause of an exudate is pneumonia (par pneumonic effusion).

- Pleural lymphocytosis is common in malignancy and tuberculosis.
- Eosinophilic pleural effusions are not always benign.
- pH should be performed in all non-purulent effusions.
- In an infected effusion a pH of <7.2 indicates the need for tube drainage.
- Amylase measurement should be requested if acute pancreatitis or rupture of the esophagus is possible (pleural fluid amylase levels are elevated if they are higher than the upper limits of normal for serum or the pleural fluid/serum ratio is >1.0).
- Iso-enzyme analysis is useful in differentiating high amylase levels secondary to malignancy or ruptured esophagus from those raised in association with abdominal pathology (if the salivary amylase is raised and oesophageal rupture is not suspected, malignancy is most likely. Pleural effusions associated with pancreatic disease usually contain pancreatic amylase).
- Malignant effusions can be diagnosed by pleural fluid cytology alone in only 60% of cases.
- If the first pleural cytology specimen is negative, this should be repeated a second time.
- Both cell blocks and fluid smears should be prepared for examination and, if the fluid has clotted, it needs to be fixed and sectioned as a histological section.

The diagnosis may be suggested by certain characteristics of the effusion. For example, obvious pus suggests empyema; lupus erythematosus cells and a ratio of pleural fluid to serum antinuclear antibody greater than 1 suggests lupus pleuritis; a high level of salivary amylase level with pleural fluid acidosis suggests esophageal rupture; and a ratio of pleural fluid hematocrit to blood hematocrit greater than 0.5 suggests hemothorax. On the basis of clinical suspicion, testing of the effusion should be selective. Despite thorough testing of pleural fluid, the cause of up to one third of pleural effusions is unknown.

### **Diagnostic imaging**

- Posterior-anterior (PA) and lateral chest radiographs should be performed in the assessment of suspected pleural effusion. The PA chest radiograph is abnormal in the presence of about 200 ml pleural fluid. However, only 50 ml of pleural fluid can produce detectable posterior costophrenic angle blunting on a lateral chest radiograph.
- Ultrasound guided pleural aspiration should be used as a safe and accurate method of obtaining fluid if the effusion is small or loculated.
- Fibrinoid septations are better visualized on ultrasound than on CT scans.
- CT scans for pleural effusion should be performed with contrast enhancement.
- In cases of difficult drainage, CT scanning should be used to delineate the size and position of located effusions.
- CT scanning can usually differentiate between benign and malignant pleural thickening.

### **Invasive investigations**

- Percutaneous pleural biopsies are of greatest value in the diagnosis of granulomatous and malignant disease of the pleura. They are performed on patients with undiagnosed exudative effusions, with non-diagnostic cytology, and a clinical suspicion of tuberculosis or malignancy. Pleural biopsy, now most commonly performed through a thoracoscope, is indicated if tuberculous involvement of the pleural space is suspected. The diagnostic rate from pleural biopsy in tuberculosis is greater than 75%, whereas pleural fluid alone has a much lower yield (<15%).

With thoracoscopy, the overall diagnostic yield is higher in pleural effusion of unknown cause, mesothelioma, and lung cancers than with pleural fluid analysis alone. Use of the thoracoscope also offers the advantage of being able to proceed to pleurodesis depending on the findings during the procedure.

- Pleural tissue should always be sent for tuberculosis culture whenever a biopsy is performed.
- In cases of mesothelioma, the biopsy site should be irradiated to stop biopsy site invasion by tumor.
- When using an Abrams' needle, at least four biopsy specimens should be taken from one site.
- When obtaining biopsies from focal areas of pleural nodularity shown on contrast enhanced CT scans, image guidance should be used.
- Image guided cutting needle biopsies have a higher yield for malignancy than standard Abrams' needle pleural biopsy.
- Thoracoscopy should be considered when less invasive tests have failed to give a diagnosis.
- Routine diagnostic bronchoscopy should not be performed for undiagnosed pleural effusion.
  
- Bronchoscopy should be considered if there is haemoptysis or clinical features suggestive of bronchial obstruction.

### **Special tests**

- If a chylothorax or pseudochylothorax is suspected, pleural fluid should be sent for measurement of triglyceride and cholesterol levels and the laboratory asked to look for the presence of cholesterol crystals and chylomicrons. True chylous effusions result from disruption of the thoracic duct or its tributaries. This leads to the presence of chyle in the pleural space. Approximately 50% are due to malignancy (particularly lymphoma), 25% trauma (especially during surgery), and the rest are miscellaneous causes such as tuberculosis, sarcoidosis, and

amyloidosis. A true chylothorax will usually have a high triglyceride level, usually  $>1.24$  mmol/l (110 mg/dl), and can usually be excluded if the triglyceride level is  $<0.56$  mmol/l (50 mg/dl). The biochemistry laboratory should be asked to look for the presence of chylomicrons between these values. Cholesterol effusions (fluid cholesterol  $>250$  mg/dL, triglyceride  $<110$  mg/dL, and absence of chylomicrons) are not true chylous effusions but are known as *pseudochylothorax*. They are seen in the setting of chronic pleural effusions and in some cases of nephrotic syndrome; the more common causes are old tuberculous effusions and rheumatoid effusions.

- If urinothorax is suspected, the pleural fluid creatinine level should be measured and will be higher than the serum creatinine level.
- When pleural biopsies are taken, they should be sent for both histological examination and culture to improve the diagnostic sensitivity for tuberculosis.
- There are no specific pleural fluid characteristics to distinguish those caused by pulmonary embolism. This diagnosis should be pursued on clinical grounds.
- Suspected rheumatoid effusions should have a pleural fluid pH, glucose and complement measured.
- Rheumatoid arthritis is unlikely to be the cause of an effusion if the glucose level in the fluid is above 1.6 mmol/l (29 mg/dl).
- The pleural fluid ANA (anti-nuclear antibody) level should not be measured as it mirrors serum levels and is therefore unhelpful.
- In patients with HIV infection, the differential diagnosis of pleural effusion is wide and differs from the immunocompetent patient.

## **COMPLICATIONS**

There is respiratory failure due to mechanical compression of lung parenchyma by large pleural effusion, congestive heart failure due to abnormal ventricular filling in case of huge pleural effusion, progressive intoxication in case of empyema of pleura.

### ***Differential Diagnosis***

Differential diagnosis is based on appearance of transudate or exudate in the pleural cavity, specific findings in pleural fluid and clinical signs of underlying etiology.

## **TREATMENT**

Treatment of transudative effusions is initially directed toward correction of the causative disorder. Treatments of exudative effusions also may deal with the underlying disorder, but pleural interventions are necessary more often.

### **Management of persistent undiagnosed pleural effusion.**

- In persistently undiagnosed effusions, the possibility of pulmonary embolism and tuberculosis should be reconsidered since these disorders are amenable to specific treatment.
- Undiagnosed pleural malignancy proves to be the cause of many “undiagnosed” effusions with sustained observation.

## MANAGEMENT OF PLEURAL INFECTION

### *Diagnostic pleural fluid sampling in par pneumonic pleural effusions*

- All patients with a pleural effusion in association with sepsis or a pneumonic illness require diagnostic pleural fluid sampling.

### *Sampling small par pneumonic pleural effusions*

- In the event of a small effusion or a failed previous attempt at pleural fluid sampling, an ultrasound scan and image guided fluid sampling is recommended.
- Pleural effusions with maximal thickness <10 mm on ultrasound scanning can be observed, with pleural fluid sampling if the effusion enlarges.

### *When to use chest tube drainage in pleural infection*

- Patients with frankly purulent or turbid/cloudy pleural fluid on sampling should receive prompt pleural space chest tube drainage.
- The presence of organisms identified by Gram stain or culture from non-purulent pleural fluid samples indicates that pleural infection is established and should lead to prompt chest tube drainage.
- Pleural fluid pH should be assessed in all non-purulent, possibly infected effusions.

- pH <7.2 indicates chest tube drainage is required.
- Para pneumonic effusions that do not fulfill these criteria for chest tube drainage should be treated with antibiotics alone provided clinical progress is good.
- Poor clinical progress during treatment with antibiotics alone should lead to prompt patient review and probably chest tube drainage.

#### *Other indications for chest tube drainage*

- Patients with a located pleural collection should receive earlier chest tube drainage.
- Large non-purulent effusions should be drained by chest tube for symptomatic benefit.

#### *Referral to a respiratory specialist*

- A respiratory physician or thoracic surgeon should be involved in the care of all patients requiring chest tube drainage for a pleural infection.

#### *Antibiotics*

- All patients should receive antibiotics.
- Where possible, antibiotics should be guided by bacterial culture results.
- Where cultures are negative, antibiotics should cover community acquired bacterial pathogens and anaerobic organisms.
- Hospital acquired empyema requires broader spectrum antibiotic cover.

#### *Chest tube drainage*

- There is no consensus on the size of the optimal chest tube for drainage.
- If a small bore flexible catheter is used, regular flushing and suction is recommended to avoid catheter blockage.

#### *Cessation of chest tube drainage in the presence of a residual pleural fluid collection*

- If the chest tube becomes blocked or pus is unable to drain, it should be flushed with saline to ensure its patency. If poor drainage persists, a chest radiograph or CT scan should be performed to check drain position.

#### *Intrapleural fibrinolytic drugs*

- Intrapleural fibrinolytic drugs (streptokinase 250 000 IU twice daily for 3 days or urokinase 100 000 IU once a day for 3 days) improve radiological outcome and hospital stay. Current best evidence favors their use, but it is not known if they reduce mortality and/or the need for surgery. Clinical trials are underway to address this question.
- Patients who receive intrapleural streptokinase should be given a streptokinase exposure card and should receive urokinase or tissue plasminogen activator (TPA) for subsequent indications.

#### *Persistent sepsis and pleural collection*

- Patients with persistent sepsis and a residual pleural collection should undergo further radiological imaging.

#### *Bronchoscopy*

- Bronchoscopy should only be performed in patients where there is a high index of suspicion of bronchial obstruction.

#### *Nutrition*

- Clinicians should ensure adequate nutritional support commencing as soon as possible after pleural infection is identified.

#### *Referral for surgical treatment*

- Failure of chest tube drainage, antibiotics and fibrinolytic drugs should prompt early discussion with a thoracic surgeon.
- Patients should be considered for surgical treatment if they have persisting sepsis in association with a persistent pleural collection, despite chest tube drainage and antibiotics.

#### *Patients not considered fit for surgery and not improving with chest tube drainage and antibiotics*

- In cases of ineffective chest tube drainage and persistent sepsis in patients unable to tolerate general anesthesia, re-imaging the thorax and placement of further image guided small bore catheters, large bore chest tubes, or intrapleural fibrinolytic therapy should be considered.

- Local anesthetic surgical rib resection should be considered in patients unsuitable for general anesthesia.

## MANAGEMENT OF MALIGNANT PLEURAL EFFUSIONS

### *Clinical presentation*

- Massive pleural effusions are most commonly due to malignancy.

### *Management by observation alone*

- Observation is recommended if the patient is asymptomatic or there is no recurrence of symptoms after initial thoracentesis.
- Advice should be sought from the thoracic malignancy multidisciplinary team for symptomatic or recurrent malignant effusions.

### *Therapeutic pleural aspiration*

- Repeat pleural aspiration is recommended for the palliation of breathlessness in patients with a very short life expectancy.
- Caution should be taken if removing more than 1.5 l on a single occasion.
- The recurrence rate at 1 month after pleural aspiration alone is close to 100%.
- Intercostal tube drainage without pleurodesis is not recommended because of a high recurrence rate.

### *Lung re-expansion, fluid drainage and suction*

- Large pleural effusions should be drained in a controlled fashion to reduce the risk of re-expansion pulmonary oedema (RPO).
- Suction to aid pleural drainage before and after pleurodesis is usually unnecessary but, if applied, a high volume, low-pressure system is recommended.
- In patients where only partial pleural apposition can be achieved, chemical pleurodesis should still be attempted and may provide symptomatic relief.
- Once effusion drainage and lung re-expansion have been radiographically confirmed, pleurodesis should not be delayed while the cessation of pleural fluid drainage is awaited.

### *Analgesia and premedication*

- Lignocaine (3 mg/kg; maximum 250 mg) should be administered intrapleurally just prior to sclerosant administration.

- Premedication should be considered to alleviate anxiety and pain associated with pleurodesis.

#### *Selecting a sclerosing agent*

- Talc is the most effective sclerosant available for pleurodesis.
- Pleuritic chest pain and fever are the most common side effects of sclerosant administration.
- In the absence of excessive fluid drainage (>250 ml/day) the intercostal tube should be removed within 12–72 hours of sclerosant administration.

#### *Intrapleural fibrinolytics*

- Intrapleural instillation of fibrinolytic drugs is recommended for the relief of distressing dyspnea due to multiloculated malignant effusion resistant to simple drainage.

#### *Thoracoscopy in malignant pleural effusion*

- Thoracoscopy should be considered for the diagnosis of suspected but unproven malignant pleural effusion.
  - Thoracoscopy should be considered for the control of recurrent malignant pleural effusion.

## **7.TASKS FOR SELF-ASSESSMENT CASE-BASED QUESTIONS**

### **- Case based questions:**

1. What is the normal function of pleural fluid?
2. What are patient's complaints with exudative pleurisy?
3. What is heard over the percussion at exudative pleurisy?
4. What is heard over the auscultation at exudative pleurisy?
5. Which type of effusion is typical for TB pleurisy?
6. Which cells are not present normally in the pleural fluid?
7. Which investigation is the most sensitive for detection of pleural effusion?
8. Which mechanism is responsible for the accumulation of pleural fluid due to pneumonia?

9. What are complications of diagnostic thoracentesis?
10. Which diseases can be accompanied by pleurisy?

1. What is the normal average amount of fluid in the pleural cavity?
  - A. 200 ml
  - B. 100 ml
  - C. 50 ml
  - D. 10 ml
  - E. 0 ml
2. Which cells are not present normally in the pleural fluid?
  - A. mesothelial cells
  - B. macrophages
  - C. lymphocytes
  - D. erythrocytes
3. What is the normal function of pleural fluid?
  - A. gases exchange
  - B. immunological defense
  - C. lubricant to facilitate respiratory movements
  - D. excretion of waste products
4. What is the most common cause of pleural effusion?
  - A. Pneumonia
  - B. Congestive heart failure
  - C. Malignancy
  - D. Tuberculosis
  - E. Pulmonary embolization
5. Which symptom is mostly specific for pleural effusion?
  - A. weight loss

B. fever

C. chest pain

D. dyspnea

E. cough

6. Which symptom is mostly specific for dry pleurisy?

A. weight loss

B. fever

C. chest pain

D. dyspnea

E. cough

7. What is the cause of chest pain due to pleurisy?

A. inflammation of the pleura

B. accumulation of the fluid in the pleural space

C. general intoxication

D. concomitant bronchitis

8. Which mechanism is not responsible for dyspnea in case of pleural effusion?

A. inflammation of the pleura

B. accumulation of the fluid in the pleural space

C. general intoxication

D. concomitant bronchitis

9. Which sign is mostly specific for identifying of pleural effusion during percussion?

A. resonant sound

B. dull sound

C. tympanic sound

10. Which investigation is the most sensitive for detection of pleural effusion?

- A. Ultrasound
- B. Chest X-ray
- C. Bronchoscopy
- D. Spirometry

11. What is the pleural empyema?

- A. inflammation of pleural layers
- B. excessive accumulation of fluid in the pleural cavity
- C. infection in the lung parenchyma
- D. infection in the pleural space

12. What is the hemothorax?

- A. accumulation of blood in the pleural cavity
- B. accumulation of air in the pleural cavity
- C. accumulation of urine in the pleural cavity
- D. accumulation of transudate in the pleural cavity

13. What is the cause of chylothorax?

- A. tuberculosis
- B. lung cancer
- C. lung gangrene
- D. trauma of the chest wall
- E. hemodialysis

14. How many cases of pneumonia are complicated by pleural effusion?

- A. 100%
- B. 80%
- C. 40%
- D. 20%
- E. 0%

15. Which mechanism is responsible for the accumulation of pleural fluid due to pneumonia?

- A. increase in hydrostatic pressure in the microvascular circulation
- B. decrease in oncotic pressure in the microvascular circulation
- C. decrease in pressure in the pleural space
- D. increased permeability of the microvascular circulation
- E. impaired lymphatic drainage from the pleural space

16. Which mechanism is responsible for the accumulation of pleural fluid due to breast cancer?

- A. increase in hydrostatic pressure in the microvascular circulation
- B. decrease in oncotic pressure in the microvascular circulation
- C. decrease in pressure in the pleural space
- D. increased permeability of the microvascular circulation
- E. impaired lymphatic drainage from the pleural space

17. Which mechanism is responsible for the accumulation of pleural fluid due to congestive heart failure?

- A. increase in hydrostatic pressure in the microvascular circulation
- B. decrease in oncotic pressure in the microvascular circulation
- C. decrease in pressure in the pleural space
- D. increased permeability of the microvascular circulation
- E. impaired lymphatic drainage from the pleural space

18. All the following criteria are used to classify transudates and exudates, except:

- A. fluid protein level  $>30$  g/l
- B. pleural fluid protein/serum protein  $>0.5$
- C. pleural level of glucose  $<2,2$  mmol/l
- D. pleural fluid LDH/serum LDH  $>0.6$
- E. pleural fluid LDH more than two-thirds normal upper limit for serum

19. Which of the following diseases does not lead to formation of pleural effusion?

- A. congestive heart failure
- B. pulmonary embolization
- C. nephrotic syndrome
- D. functional non-ulcer dyspepsia
- E. mesothelioma

20. The complications of diagnostic thoracentesis are all of the following, except:

- A. pneumothorax
- B. spleen or liver puncture
- C. congestive heart failure
- D. bleeding (local, intrapleural, or intra-abdominal)
- E. empyema.

## **8.CASE-BASED QUESTIONS**

### **Task 1.**

28-years old male known to be drug dependent complains on cough, chest pain that is exacerbated by inhaling, shortness of breath, weakness, fever - 39.9° C. He was treated at home, feeling progressively worse and finally at 4-day hospitalized. The condition is severe. Skin is pale, respiration rate - 26/min, HR - 108/min, BP - 105/80 mmHg. There is dull sound on percussion below the angle of the right scapula and absence of any sound in this area on auscultation. Cardiac rhythm is regular, tachycardia. What is the most likely diagnosis?

- A. pneumonia
- B. lung gangrene
- C. lung abscess
- D. bronchiectasis
- E. exudative pleurisy

**Task 2.**

40-years male complains on increasing body temperature to 39.5°C, cough with release of "rusty" sputum, shortness of breath. Respiration rate - 32/min. There are dull sound at percussion and crepitation at auscultation on the lower part of the right lung. Blood test: leucocytes -  $14 \times 10^9/l$ , ESR - 35 mm/h. What is the preliminary diagnosis?

- A. pleural effusion
- B. Bronchiectasis
- C. Tuberculosis of the lungs
- D. Acute bronchitis
- E. Pneumonia

**Task 3.**

In 46-years old male patient with pleural effusion of unknown etiology the diagnostic pleural puncture was made. Analysis of fluid revealed protein – 5 g/l, LDH (fluid/blood) – 0.1, hematocrit – 1%. Which disease may be the possible causative factor for pleural effusion?

- A. lung cancer
- B. para-pneumonic effusion
- C. mesothelioma
- D. tuberculosis
- E. heart failure

**Task 4.**

50-years old male was admitted to hospital with complaints on increasing of body temperature to 38.5° C, severe weakness, pain in the chest, dry cough during 9 day. Respiration rate - 28/min. Pulse - 100/min. There are bronchial sound at auscultation and dull sound at percussion in the lower part of right lung. After 5 days there was an attack of coughing with the release of 200 ml of purulent sputum, after which the body temperature decreased. X-ray reveled rounded focal opacity with horizontal fluid level. What is the diagnosis?

- A. cyst of lung

- B. acute lung abscess
- C. lung cancer
- D. pneumonia
- E. pleural empyema

**Task 5.**

68-years old male patient complains on cough, increased body temperature to 37.5° C, chest pain when breathing. There was chest trauma 5 days ago. On examination: paleness, lagging the left half of the chest during breathing. Auscultation - weakened vesicular breathing and pleural friction rub in the lower left part of the chest. Blood analysis revealed: leukocytosis, increased ESR. X-ray - enhanced pulmonary pattern. What is the clinical diagnosis?

- A. dry pleurisy
- B. pneumonia
- S. pleural effusion
- D. pneumothorax
- E. lung cancer

**Task 6.**

48-years old female with long history of alcohol abuse was admitted to hospital due to progressive dyspnea. X-ray examination revealed right-sided pleural effusion. Diagnostic pleural puncture was performed. Which cause of a pleural effusion probably can be considered if the pleural fluid total protein is <30 g/l?

- A. Liver cirrhosis
- B. Lung cancer
- C. Tuberculosis
- D. Systemic lupus erythematosus
- E. Acute pancreatitis

**Task 7.**

71-years old female was preliminary diagnosed having pleural effusion of unknown etiology. To establish underlying etiology diagnostic pleural puncture is required. All of the following are contraindications for thoracentesis, except?

- A. bleeding diathesis
- B. anticoagulation therapy
- C. small amount of pleural fluid
- D. mechanical ventilation
- E. arterial hypertension

**Task 8.**

27-years old male was hospitalized with symptoms of cough, fever (38°C), chest pain and mild dyspnea (respiration rate – 22/min). X-ray and ultrasound examinations revealed signs of pneumonia and small ipsilateral pleural effusion (~400 ml). Analysis of pleural fluid: nonpurulent, pH – 7,35, glucose 4,3 mmol/l, LDH – 700 IU/l. What is the treatment strategy?

- A. drainage of the pleural space and antibiotics
- B. lobectomy and antibiotics
- C. postural drainage and antibiotics
- D. wide-spectrum antibiotics alone

**Task 9.**

46-years old male was hospitalized with symptoms of severe weakness, nonproductive cough, fever (39,5°C) and moderate dyspnea (respiration rate – 26/min). X-ray and ultrasound examinations revealed signs of pneumonia and moderate ipsilateral pleural effusion (~900 ml). Analysis of pleural fluid: purulent, pH – 7,1, glucose 2,0 mmol/l, LDH – 1200 IU/l. What is the treatment strategy?

- A. drainage of the pleural space and antibiotics
- B. lobectomy and antibiotics
- C. postural drainage and antibiotics
- D. wide-spectrum antibiotics alone

**Task 10.**

59-years old female underwent clinical examination because of dyspnea. X-ray revealed massive right-sided pleural effusion. Mammography revealed tumor of the right mammary gland. Which treatment is not indicated for this patient?

- A. therapeutic pleural aspiration 31

- B. antibiotics
- C. pleurodesis
- D. intrapleural fibrinolytics

**9. Further reading:**

**Main reference:**

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**Methodical recommendations are analyzed and approved at the sub-faculty meeting of the Department:**

**With the changes and additions:**

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