

МІНІСТЕРСТВО ОХОРОНИ ЗДОРОВ'Я УКРАЇНИ
Харківський національний медичний університет

Modul 3. Current practice of internal medicine.
Meaningful module №4.
Keeping patients in pulmonological clinic.
Theme 6. Management of patients
with pleural effusion

Guidelines for students and interns

Модуль 3. Сучасна практика внутрішньої медицини.
Змістовний модуль №4.
Введення хворих у пульмонологічній клініці.
Тема 6. Ведення хворих
з плевральним випотом

Методичні вказівки
для студентів та лікарів-інтернів

Рекомендовано
вченою радою ХНМУ.
Протокол № 11 від 21.12.2011.

Харків
ХНМУ
2012

Module 3. Current practice of internal medicine. Meaningful module №4. Keeping patients in pulmonological clinic. Theme 6. Management of patients with pleural effusion / comp. Oleg Babak, Galyna Fadeyenko, Valeriya Nemtsova et al. –Kharkiv: KNMU, 2012. – 24 p.

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Модуль 3. Сучасна практика внутрішньої медицини. Змістовний модуль № 4. Ведення хворих в пульмонологічній клініці. Тема 6. Ведення хворих з плевральним випотом: метод. вказ. для студентів та лікарів-інтернів / упор. О.Я. Бабак, Г.Д. Фадеєнко, В.Д.Немцова та ін. – Харків: ХНМУ, 2012. – 24 с.

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General Outcome

The students should be able to describe clinical presentation, provide the diagnose, differentials and treatment of pleurisy

The aim of this topic is to provide the student with an opportunity to:

- Provide a basic overview of the pathophysiology, history, and the main causes of pleurisy.
- Provide a diagnostic steps for the patients with suspected pleural effusion
- Provide a classification of transudates and exudates.
- Assess the results of labs and images in different variants of pleural effusion.
- Discuss the procedure of diagnostic and therapeutic thoracentesis (goals, indications, contraindication, technique of the procedure).
- Discuss the treatment (medical and surgical care) of different types of pleurisy.

Specific Learning Outcomes:

Upon successful completion of this unit, the students should be able to:

1. List and describe the main causes of pleural effusion and its classifications.
2. Explain the pathophysiology of pleural effusion.
3. Describe the most common symptoms associated with pleural effusion. List and describe anti-anginal and anti-ischemic drugs and give specific examples of each.
4. Explain the results of pleural fluid lab tests.

Specification of the theoretical question for training of Management of patients with pleural effusion.

Student must know:

1. What are the differences between exudates and transudate?
2. What diseases are associated with transudative pleural effusions?
3. What diseases are associated with exudative pleural effusions?
4. What are the main symptoms of exudative pleurisy?
5. What are the main symptoms of dry pleurisy?
6. What diseases could be suspected in case of Pleural fluid lymphocytosis?
7. What labs findings supports the diagnosis of TB pleuritis?
8. What complications of diagnostic thoracentesis could developed?
9. In which cases of pleural effusion Chest CT scanning with contrast should be performed?
10. In which cases pleurodesis could be performed?

**TESTS AND ASSIGNMENTS FOR SELF-ASSESSMENT BASIC
LEVEL OF KNOWLEDGE: MULTIPLE CHOICE QUESTIONS
(CHOOSE THE CORRECT ANSWER/STATEMENT)**

1. The chest is slightly larger but moves less on the right^ the percussion note is less resonant on the left where breath sounds are louder. The most likely diagnoses is:

- A. Consolidation on the left.
- B. Pneumothorax on the right.
- C. Collapse on the left.
- D. Consolidation on the left.
- E. Pleural effusion.

2. In the coal miner aged 50 years, a persistent blood-stained effusion is most likely to be due to:

- A. Pulmonary tuberculosis.
- B. Coal miner's pneumoconiosis.
- C. Carcinoma of the lung.
- D. Silicosis.
- E. Mesothelioma.

3. A 37- years- old male complaining of acute pain in the left half of the chest, shortness of breath, aggravated by any movements. Suddenlyfellillafter the intensive physical work. Objectively: moderate face cyanosis, left half of the chest behind the act of breathing. On percussion: left side – tympanic sound, weakened breathing. RR-24/min. Weak heart sounds. HR-90/min. On the X-ray - visible line of visceral pleura, outside of it pulmonary picture is absent. What is the most likely diagnosis?

- A. Myocardial infarction.
- B. Left-side pneumonia.
- C. Left-side exudative pleurisy.
- D. Pulmonary embolism.
- E. Spontaneous pneumothorax.

4. The patient complains of acute shortness of breath which increases with exercise. This compliances appeared suddenly 2 hours ago at work: sharp pain in left chest, cough. The pain decreased, but increased shortness of breath, dizziness, paleness, cold sweat, cyanosis. Lack of vesicular breathing, radiography - darkness on the left. What kind of pathology can be suspected?

- A. Spontaneous left-side pneumothorax.
- B. Lung infarction.
- C. Pleurisy.
- D. Left-side pneumonia .
- E. Lung abscess.

5. In 35 years old man while rising weights appeared sharp pain in the left half of the chest. The worsening of condition progressed, increased shortness of breath, weakness, dizziness. On percussion - left tympanitauscultatory - no breathing. What is the most likely diagnosis?

- A. Pleural effusion.
- B. Pulmonary embolism.
- C. Pneumothorax.
- D. Sinistral pectoral radiculitis.
- E. Myositis.

6. The following are clinical features of a large pulmonary embolism.

- A. Pleuritic chest pain.
- B. Haemoptysis.
- C. High fever.
- D. Bradycardia.
- E. Collapsed neck veins.

7. The prevalence of lymphocytes in pleural effusion is typical for

- A. the allergic pleurisy.
- B. tuberculous or tumorous pleurisy. *
- C. for pleurisy in pulmonary infarction.
- D. for pleurisy in pneumonia.
- E. for pleurisy in uremia.

8. Bilateral effusion in the pleural cavity occurs as well

- A. In hemorrhagic vasculitis.
- B. In dermatomyositis.
- C. In congestive heart failure.
- D. In postinfarction syndrome .
- E. In diffuse pleural mesothelioma.

ANSWERS:

1	2	3	4	5	6	7	8
B	C	E	A	C	A, B	B	C

THE MANAGEMENT OF THE PATIENTS WITH PLEURISY

Pleurisy (also known as pleuritis) is an inflammation of the pleura. Approximately 1 million pleural effusions are diagnosed in the United States each year. The clinical importance of pleural effusions ranges from incidental manifestations of cardiopulmonary diseases to symptomatic inflammatory or malignant diseases, as shown in the image below, requiring urgent evaluation and treatment.

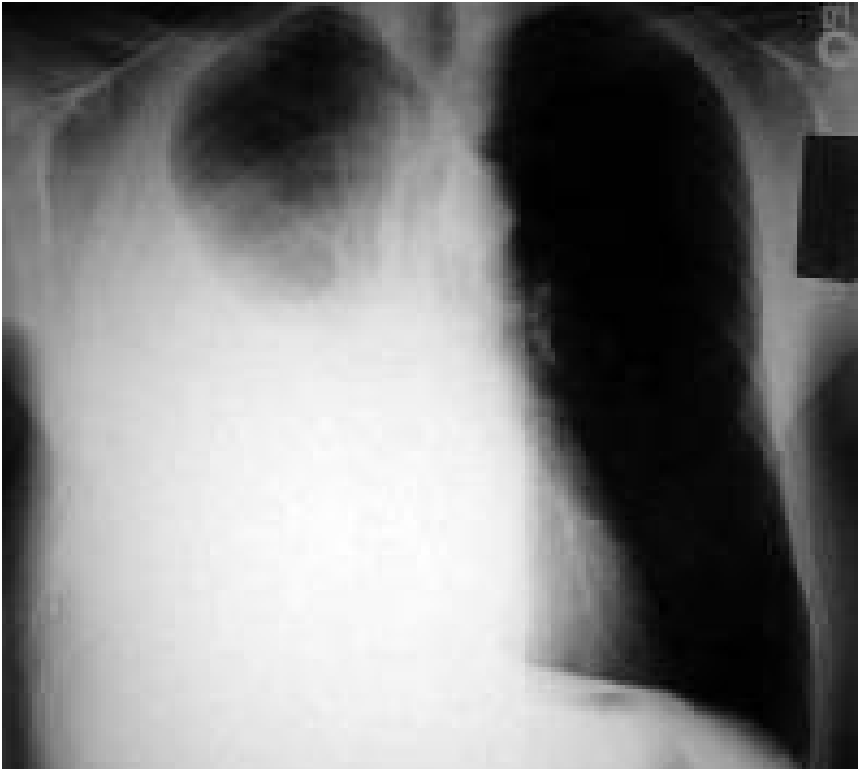


Image 1. *Large, malignant, right-sided pleural effusion.*

Pathophysiology. The normal pleural space contains approximately 1 mL of fluid, representing the balance between (1) hydrostatic and oncotic forces in the visceral and parietal pleural vessels and (2) extensive lymphatic drainage. Pleural effusions result from disruption of this balance.

Frequency. The estimated prevalence of pleural effusion is 320 cases per 100,000 people in industrialized countries, with a distribution of etiologies related to the prevalence of underlying diseases.

History. Dyspnea is the most common symptom associated with pleural effusion and is related more to distortion of the diaphragm and chest wall during respiration than to hypoxemia. In many patients, drainage of pleural fluid alleviates symptoms despite limited improvement in gas exchange

Underlying intrinsic lung or heart disease, obstructing endobronchial lesions, or diaphragmatic paralysis can also cause dyspnea, especially after coronary artery bypass surgery. Drainage of pleural fluid may partially relieve symptoms but, as importantly, may allow the underlying disease to be recognized on repeat chest radiographs.

Less common symptoms from pleural effusions include mild nonproductive cough or chest pain (sharp or stabbing pain in the chest that gets worse with deep breathing, coughing or sneezing). The pain may stay in one place, or it may spread to the shoulder or back. Sometimes it becomes a fairly constant dull ache.

Other symptoms may suggest the etiology of the pleural effusion. For example, more severe cough or production of purulent or bloody sputum suggests an underlying pneumonia or endobronchial lesion. Constant chest wall pain may reflect chest wall invasion by bronchogenic carcinoma or malignant mesothelioma. Pleuritic chest pain suggests either pulmonary embolism or an inflammatory pleural process. Persistent systemic toxicity evidenced by fever, weight loss, and inanition suggests empyema.

Causes

Transudates are usually ultrafiltrates of plasma in the pleura due to imbalance in hydrostatic and oncotic forces in the chest. However, they can also be caused by the movement of fluid from peritoneal spaces or by iatrogenic infusion into the pleural space from misplaced or migrated central venous catheters or nasogastric feeding tubes. *Transudates* are caused by a small, defined group of etiologies, including the following:

- Congestive heart failure.
- Cirrhosis (hepatic hydrothorax).
- Atelectasis (which may be due to malignancy or pulmonary embolism).
- Hypoalbuminemia.
- Nephrotic syndrome.
- Peritoneal dialysis.
- Myxedema.
- Constrictive pericarditis.

In contrast, exudates are produced by a variety of inflammatory conditions and often require more extensive evaluation and treatment. Exudates arise from pleural or lung inflammation, from impaired lymphatic drainage of the pleural space, and from transdiaphragmatic movement of inflammatory fluid from the peritoneal space. The more common causes of *exudates* include the following:

- Parapneumonic causes.
- Malignancy (carcinoma, lymphoma, mesothelioma).

- Pulmonary embolism.
- Collagen-vascular conditions (rheumatoid arthritis, lupus).
- Tuberculous.
- Asbestos exposure.
- Pancreatitis.
- Trauma.
- Postcardiac injury syndrome.
- Esophageal perforation.
- Radiation pleuritis.
- Drug use.
- Chylothorax.
- Meigs syndrome.
- Sarcoidosis.
- Yellow nail syndrome.

Some cases of pleurisy are idiopathic, meaning the cause cannot be determined.

Diagnosis

A diagnosis of pleurisy or another pleural condition is based on medical histories, physical exams, and diagnostic tests. The goals are to rule out other sources of the symptoms and to find the cause of the pleurisy so the underlying disorder can be treated (table).

Table 3 – Characteristics of transudative pleural effusions*

Cause	Clinical features/comments
CHF	Mesothelial cells and lymphocytes predominate; thoracentesis indicated if fever, pleurisy, normal heart size, or unilateral effusion is present
Cirrhosis	Patients usually have obvious ascites; effusions are right-sided in 70%
Nephrotic syndrome	Usually bilateral; rule out embolus, especially if effusion is unilateral or if bilateral effusions are disparate in size
Pericardial disease	Usually left-sided; one third are bilateral
Atelectasis	Common in medical ICU and postoperative patients; usually small and unilateral
Peritoneal dialysis	Usually small and bilateral; occasionally unilateral and massive; pleural fluid protein concentration less than 1 g/dL; pleural fluid glucose concentration greater than 300 mg/dL
Urinothorax	Found ipsilateral to obstructed kidney; usually small to moderate, with odor of urine; resolves with relief of urinary obstruction

CHF, congestive heart failure.

*About 20% of effusions caused by pulmonary embolism are transudates; about 30% of those caused by sarcoidosis are transudates.

Physical exam

Physical findings, which do not usually manifest until pleural effusions exceed 300 mL, include the following:

- Decreased breath sounds.
- Dullness to percussion.
- Decreased tactile fremitus.
- Egophony (E-to-A change).
- Pleural friction rub.

• Mediastinal shift away from the effusion: This is observed with effusions of greater than 1000 mL. Displacement of the trachea and mediastinum toward the side of the effusion is an important clue to obstruction of a lobar bronchus by an endobronchial lesion, which can be due to malignancy or, less commonly, a nonmalignant cause such as a foreign body.

Diagnostic tests

Laboratory Studies. Thoracentesis should be performed for new and unexplained pleural effusions when sufficient fluid is present to allow a safe procedure. Observation of pleural effusion(s) is reasonable when benign etiologies are likely, such as in the setting of overt congestive heart failure, viral pleurisy, or recent thoracic or abdominal surgery. Laboratory testing helps distinguish pleural fluid transudates from exudates; however, certain types of exudative pleural effusions might be suspected simply by observing the gross characteristics of the fluid obtained during thoracentesis:

- Frankly purulent fluid indicates an empyema.
- A putrid odor suggests an anaerobic empyema.
- A milky, opalescent fluid suggests a chylothorax, resulting most often from lymphatic obstruction by malignancy or thoracic duct injury by trauma or surgical procedures.
- Grossly bloody fluid may result from trauma, malignancy, postpericardiotomy syndrome, and asbestos-related effusion, and this indicates the need for a spun hematocrit test of the sample. A pleural fluid hematocrit level of more than 50% of the peripheral hematocrit level defines a hemothorax, which often requires tube thoracostomy.

The initial diagnostic consideration is distinguishing transudates from exudates. Although a number of chemical tests have been proposed to differentiate pleural fluid transudates from exudates, the tests first proposed by Light et al have become the criterion standards.

The fluid is considered an exudate if any of the following apply:

- Ratio of pleural fluid to serum protein greater than 0,5.
- Ratio of pleural fluid to serum lactate dehydrogenase (LDH) greater than 0,6.
- Pleural fluid LDH greater than two thirds of the upper limits of normal serum value.

These criteria require simultaneous measurement of pleural fluid and serum protein and LDH. However, a meta-analysis of 1448 patients suggested that the following combined pleural fluid measurements might have sensitivity and specificity comparable to the criteria from Light et al for distinguishing transudates from exudates:

- Pleural fluid LDH value greater than 0.45 of the upper limit of normal serum values.

- Pleural fluid cholesterol level greater than 45 mg/dL.

- Pleural fluid protein level greater than 2.9 g/dL.

Clinical judgment is required when pleural fluid test results fall near the cutoff points.

The criteria from Light et al and these alternative criteria identify nearly all exudates correctly, but they misclassify approximately 20-25% of transudates as exudates, usually in patients on long-term diuretic therapy for congestive heart failure because of the concentration of protein and LDH within the pleural space due to diuresis. Using the criterion of serum minus pleural protein concentration level of less than 3.1 g/dL, rather than a serum/pleural fluid ratio of greater than 0.5, more correctly identifies exudates in these patients.

Although pleural fluid albumin is not typically measured, a gradient of serum albumin to pleural fluid albumin less than 1.2 g/dL also identifies an exudate in such patients.

In addition, studies suggest that pleural fluid levels of N-terminal pro-brain natriuretic peptide (NT-proBNP) are elevated in effusions due to congestive heart failure. More recently, elevated pleural NT-proBNP was shown to out-perform pleural fluid BNP as a marker of heart failure-related effusion. Thus, at institutions where this test is available, high pleural levels of NT-proBNP (defined in different studies as >1300-4000 ng/L) may help to confirm heart failure as the cause of an otherwise idiopathic chronic effusion.

Pleural fluid LDH. Pleural fluid LDH levels greater than 1000 IU/L suggest empyema, malignant effusion, rheumatoid effusion, or pleural paragonimiasis. Pleural fluid LDH levels are also increased in effusions from *Pneumocystis jirovecii* pneumonia; the diagnosis is suggested by a pleural fluid/serum LDH ratio greater than 1, with a pleural fluid/serum protein ratio less than 0.5.

Pleural fluid glucose and pH. In addition to these tests, glucose and pleural fluid pH should be measured during the initial thoracentesis in most situations.

A low pleural glucose concentration (30-50 mg/dL) suggests malignant effusion, tuberculous pleuritis, esophageal rupture, or lupus pleuritis, and a very low pleural glucose concentration (ie, <30 mg/dL).

- further restricts diagnostic possibilities to rheumatoid pleurisy or empyema.

- Handle pleural fluid samples as carefully as arterial samples for pH measurements, with fluid collected in heparinized syringes and ideally trans-

ported on ice for measurement within 6 hours. However, studies have shown that when collected in heparinized syringes, pleural fluid pH does not change significantly even at room temperature over several hours. Consequently, if appropriately collected samples can be processed quickly, pH measurements should not be canceled simply because the sample was not transported on ice.

- Pleural fluid pH is highly correlated with pleural fluid glucose levels. Pleural fluid pH less than 7.30 with a normal arterial blood pH level is caused by the same diagnoses as listed above for low pleural fluid glucose. However, for parapneumonic effusions, a low pleural fluid pH level is more predictive of complicated effusions (that require drainage) than is a low pleural fluid glucose level.

- In parapneumonic effusions, pleural fluid pH less than 7.1-7.2 indicates the need for urgent drainage of the effusion, and pleural fluid pH more than 7.3 suggests that the effusion may be managed with systemic antibiotics alone.

- In malignant effusions, pleural fluid pH less than 7.3 has been associated in some reports with more extensive pleural involvement, higher yield on cytology, decreased success of pleurodesis, and shorter survival times.

Pleural fluid cell count differential

If an exudate is suspected clinically or is confirmed by chemistry test results, send the pleural fluid for total and differential cell counts, Gram stain, culture, and cytology.

- Pleural fluid lymphocytosis, with lymphocyte values greater than 85% of the total nucleated cells, suggests tuberculosis (TB), lymphoma, sarcoidosis, chronic rheumatoid pleurisy, yellow nail syndrome, or chylothorax. Pleural lymphocyte values of 50-70% of the nucleated cells suggest malignancy.

Pleural fluid eosinophilia (PFE), with eosinophil values greater than 10% of nucleated cells, is seen in approximately 10% of pleural effusions and is not correlated with peripheral blood eosinophilia. PFE is most often caused by air or blood in the pleural space. Blood in the pleural space causing PFE may be the result of pulmonary embolism with infarction or benign asbestos pleural effusion. PFE may be associated with other nonmalignant diseases, including parasitic.

- disease (especially paragonimiasis), fungal infection (coccidioidomycosis, cryptococcosis, histoplasmosis), and a variety of medications. The presence of PFE does not exclude a malignant effusion, especially in patient populations with a high prevalence of malignancy. The presence of PFE makes tuberculous pleurisy unlikely and makes the progression of a parapneumonic effusion to an empyema unlikely.

- Mesothelial cells are found in variable numbers in most effusions, but their presence at greater than 5% of total nucleated cells makes a diagnosis of TB less likely.

- Markedly increased numbers of mesothelial cells, especially in bloody or eosinophilic effusions, suggests pulmonary embolism as the cause.

Pleural fluid culture and cytology. Culture of infected pleural fluid yields positive results in approximately 60% of cases, and even less often for anaerobic organisms. Diagnostic yields may be increased by directly culturing pleural fluid into anaerobic blood culture bottles.

Malignancy is suspected in patients with known cancer or with lymphocytic, exudative effusions, especially when bloody. Direct tumor involvement of the pleura is diagnosed most easily by performing pleural fluid cytology.

- Heparinize samples (1 mL of 1:1000 heparin per 50 mL of pleural fluid) if bloody, and refrigerate if samples will not be processed within 1 hour.

- The reported diagnostic yields of cytology vary from 60-90%, depending on the extent of pleural involvement and the type of primary malignancy.

- The sensitivity of cytology is not highly related to the volume of pleural fluid tested; sending more than 50-60 mL of pleural fluid for cytology does not increase the yield of direct cytospin analysis, and volumes of approximately 150 mL are sufficient when both cytospin and cell block preparations are analyzed.

- Cytology findings are positive in 58% of effusions related to mesothelioma.

- Tumor markers, such as carcinoembryonic antigen, Leu-1, and mucin, are suggestive of malignant effusions (especially adenocarcinoma) when pleural fluid values are very high; however, because of low sensitivity, they are not helpful if values are normal or only modestly increased.

Suspect TB pleuritis in patients with a history of exposure or a positive purified protein derivative (PPD) finding and in patients with lymphocytic exudative effusions, especially if less than 5% mesothelial cells are detected on differential blood cell counts.

- Because most tuberculous pleural effusions probably result from a hypersensitivity reaction to the *Mycobacterium* rather than from microbial invasion of the pleura, acid-fast bacillus stains of pleural fluid are rarely diagnostic (<10% of cases), and pleural fluid cultures grow *Mycobacterium tuberculosis* in less than 65% of cases.

- In contrast, the combination of histology and culture of pleural tissue obtained by pleural biopsy increases the diagnostic yield to 90%.

- Adenosine deaminase (ADA) activity of greater than 43 U/mL in pleural fluid supports the diagnosis of TB pleuritis. However, the test has a sensitivity of only 78%; therefore, pleural ADA values less than 43-50 U/mL do not exclude the diagnosis of TB pleuritis.

- Interferon-gamma concentrations in pleural fluid greater than 140 pg/mL also support the diagnosis of TB pleuritis, but this test is not routinely available.

Additional tests. Additional specialized tests are warranted when specific etiologies are suspected.

- Measure pleural fluid amylase levels if a pancreatic origin or ruptured esophagus is suspected, or if a unilateral left-sided pleural effusion remains undiagnosed after initial testing. Of note, increased pleural fluid amylase can also be seen with malignancy. An additional assay of amylase isoenzymes can help distinguish a pancreatic source (diagnosed by elevated pleural fluid pancreatic isoenzymes) from other etiologies.

- Measure triglyceride and cholesterol levels in milky pleural fluids when chylothorax or pseudochylothorax is suspected.

- Consider immunologic studies, including pleural fluid antinuclear antibody and rheumatoid factor, when collagen-vascular diseases are suspected.

Idiopathic exudative effusions. Despite primary evaluation with repeated diagnostic thoracenteses, approximately 20% of exudative effusions remain undiagnosed. Clues to the diagnosis that may have been overlooked include (1) occupational exposure to asbestos 10-20 years earlier, which may suggest benign asbestos effusion; (2) medication exposure to nitrofurantoin, amiodarone, or medications associated with a drug-induced lupus syndrome; and (3) hepatic hydrothorax unrecognized in a patient with minimal or undetectable ascites.

Chest CT scanning with contrast should be performed in all patients with an undiagnosed pleural effusion. What lab findings supports the diagnosis of TB pleuritis?, if not previously performed, to detect thickened pleura or signs of invasion of underlying or adjacent structures. The 2 diagnostic imperatives in this situation are pulmonary embolism and tuberculous pleuritis. In both cases, the pleural effusion is a harbinger of potential future morbidity. In contrast, a short delay in diagnosing metastatic malignancy to the pleural space has less impact on future clinical outcomes.

CT angiography should be ordered if pulmonary embolism is strongly suggested.

Pleural biopsy should be considered, especially if TB or malignancy is suggested. Medical thoracoscopy with the patient under conscious sedation and local anesthesia has emerged as a diagnostic tool to directly visualize and take a biopsy specimen from the parietal pleura in cases of undiagnosed exudative effusions. As an alternative, closed-needle pleural biopsy is a blind technique that can be performed at the patient's bedside. Medical thoracoscopy has a higher diagnostic yield for malignancy; closed-needle pleural biopsy findings aid in diagnosis of only 7-12% of malignant effusions when cytology findings alone are negative. However, the yield of closed-needle pleural biopsy (histology plus culture) is as high as thoracoscopy for TB pleuritis and is a useful alternative procedure for this diagnosis when available.

Among patients with undiagnosed pleural effusions after the primary evaluation, those who meet all 6 of the following clinical parameters are predicted to have a benign course, and no further evaluation is necessary.

- Patients are clinically stable.
- Patients do not have weight loss.
- The results of the PPD test are negative and the pleural ADA value is less than 43 U/mL.
- The patient does not have a fever.
- The pleural fluid differential blood cell count has less than 95% lymphocytes.
- The effusion occupies less than 50% of the hemithorax.

For other patients with undiagnosed exudative effusions, approximately 20% have a specific etiology determined, including malignancy. For such patients, weigh the benefits and risks of pursuing a diagnostic strategy that will involve using progressively more invasive procedures, given the low likelihood of finding a curable etiology.

- Consider bronchoscopy only if a patient has parenchymal abnormalities or hemoptysis.

Surgical approaches to the diagnosis of pleural effusions include.

- thoracoscopy (pleuroscopy) and open thoracotomy, which reveal an etiology in 92% of effusions that remain undiagnosed after a medical evaluation.
- Where available, medical thoracoscopy may be both diagnostic and therapeutic; complete drainage of the effusion and talc sclerosis can be performed at the time of the procedure.
- Note that in most medical centers, surgical exploration using thoracoscopy or thoracotomy entails the risks of general anesthesia and is probably warranted only in patients who are symptomatic and anxious for a (potentially incurable) diagnosis.

Imaging Studies

Chest radiograph. Effusions of more than 175 mL are usually apparent as blunting of the costophrenic angle on upright posteroanterior chest radiographs. On supine chest radiographs, which are commonly used in the intensive care setting, moderate-to-large pleural effusions may appear as a homogenous increase in density spread over the lower lung fields on a supine chest radiograph. Apparent elevation of the hemidiaphragm, lateral displacement of the dome of the diaphragm, or increased distance between the apparent left hemidiaphragm and the gastric air bubble suggests subpulmonic effusions. Note the image 2. below.

Lateral decubitus films more reliably detect smaller pleural effusions. Layering of an effusion on lateral decubitus films defines a freely flowing effusion and, if the layering fluid is 1 cm thick, indicates an effusion of greater than 200 mL that is amenable to thoracentesis. Failure of an effusion to layer on lateral decubitus films indicates loculated pleural fluid or some other etiology causing the increased pleural density. Note the image 3. below.



Image 2. Chest radiograph showing left-sided pleural effusion



Image 3. Left lateral decubitus film showing freely layering pleural effusion

Procedures

Diagnostic thoracentesis. Perform diagnostic thoracentesis if the etiology of the effusion is unclear or if the presumed cause of the effusion does not respond to therapy as expected. Pleural effusions *do not require thoracentesis* if they are too small to safely aspirate or, in clinically stable patients, if their presence can be explained by underlying congestive heart failure (especially bilateral effusions) or by recent thoracic or abdominal surgery. *Relative contraindications* to diagnostic thoracentesis include a small volume of fluid (<1 cm thickness on a lateral decubitus film), bleeding diathesis or systemic anticoagulation, mechanical ventilation, and cutaneous disease over the proposed puncture site. Mechanical ventilation with positive end-expiratory pressure does not increase the risk of pneumothorax after thoracentesis, but it increases the likelihood of severe complications (tension pneumothorax or persistent bronchopleural fistula) if the lung is punctured. *Complications* of diagnostic thoracentesis include pain at the puncture site, cutaneous or internal bleeding, pneumothorax, empyema, and spleen/liver puncture. Pneumothorax complicates approximately 12-30% of thoracenteses but requires treatment with a chest tube in less than 5% of cases. Use of needles larger than 20 gauge increases the risk of a pneumothorax complicating the thoracentesis. In addition, significant chronic obstructive or fibrotic lung disease increases the risk of a symptomatic pneumothorax complicating the thoracentesis.

In patients with large, freely flowing effusions and no relative contraindications to thoracentesis, diagnostic thoracentesis can usually be performed safely, with the puncture site initially chosen based on the chest radiograph and located at 1-2 rib interspaces below the level of dullness to percussion on physical examination. In other situations, ultrasound or chest CT imaging should be used to guide thoracentesis.

After the site is disinfected with chlorhexidine (preferred) or povidone/iodine (no longer recommended) solution and sterile drapes are placed, anesthetize the skin, periosteum, and parietal pleura with 1% lidocaine through a 25-gauge needle. If pleural fluid is not obtained with the shorter 25-gauge needle, continue anesthetizing with a 1.5-inch, 22-gauge needle; for patients with larger amounts of subcutaneous tissue, a 3.5-inch, 22-gauge spinal needle with inner stylet removed can be used to anesthetize the deeper tissues and find the effusion. Confirm the correct location for thoracentesis by aspirating pleural fluid through the 25- or 22-gauge needle before introducing larger-bore thoracentesis needles or catheters. If pleural fluid is not easily aspirated, stop the procedure and use ultrasound or chest CT imaging to guide thoracentesis.

When possible, patients should sit upright for thoracentesis. Patients should not lean forward because this causes pleural fluid to move to the anterior costophrenic space and increases the risk of puncture of the liver or spleen. For debilitated and ventilated patients who cannot sit upright, obtain pleural fluid by puncturing over the eighth rib at the mid-to-posterior axillary line. Such patients may require imaging to guide thoracentesis.

Supplemental oxygen is often administered during thoracentesis, both to offset hypoxemia produced by changes in ventilation-perfusion relationships as fluid is removed and to facilitate reabsorption of pleural air if pneumothorax complicates the procedure.

The frequency of complications from thoracentesis is lower when a more experienced clinician performs the procedure and when ultrasound guidance is used. Consequently, a skilled and experienced clinician should perform thoracentesis in patients who have a higher risk of complications or relative contraindications for thoracentesis and for those patients who cannot sit upright. Postprocedure expiratory chest radiographs to exclude pneumothorax are not needed in asymptomatic patients after uncomplicated procedures (single needle pass without aspiration of air). However, postprocedure inspiratory chest radiographs are recommended to establish a new baseline for patients likely to have recurrent symptomatic effusions.

Therapeutic thoracentesis. Therapeutic thoracentesis to remove larger amounts of pleural fluid is used to alleviate dyspnea and to prevent ongoing inflammation and fibrosis in parapneumonic effusions. In addition to the precautions listed for diagnostic thoracentesis, there are 3 additional considerations when performing therapeutic thoracentesis.

First, to avoid producing a pneumothorax during the removal of large quantities of fluid, remove fluid during therapeutic thoracentesis with a catheter introduced into the pleural space rather than through a sharp needle. Various specially designed thoracentesis trays are available for introducing small catheters into the pleural space. Alternatively, newer systems using spring-loaded, blunt-tip needles that avoid lung puncture are also available.

Second, monitor oxygenation closely during and after thoracentesis because arterial oxygen tension paradoxically might worsen after pleural fluid drainage due to shifts in perfusion and ventilation in the reexpanding lung. Consider use of empiric supplemental oxygen during the procedure.

Third, only remove moderate amounts of pleural fluid to avoid reexpansion pulmonary edema and to avoid causing a pneumothorax.

- Removal of 400-500 mL of pleural fluid is often sufficient to alleviate shortness of breath. The recommended limit is 1000-1500 mL in a single thoracentesis procedure.

- Larger amounts of pleural fluid can be removed if pleural pressure is monitored by pleural manometry and is maintained above -20 cm water. However, this monitoring is rarely used by most proceduralists.

- The onset of chest pressure or pain during the removal of fluid indicates a lung that is not freely expanding, and the procedure should be stopped immediately to avoid reexpansion pulmonary edema. In contrast, cough frequently occurs during removal of fluid, and this is not an indication to stop the procedure, unless the cough is causing the patient discomfort.

- The position of the mediastinum on the chest radiograph may predict whether a patient is likely to benefit from the procedure. A mediastinal shift away from the pleural effusion indicates a positive pleural pressure and compression of the underlying lung that can be relieved by thoracentesis. Note the image 5. below.

- In contrast, a mediastinal shift towards the side of the effusion indicates lung entrapment by extensive pleural involvement or endobronchial obstruction that prevents reexpansion of the lung when the pleural fluid is removed, or a trapped lung from encasement by chronic pleural thickening.

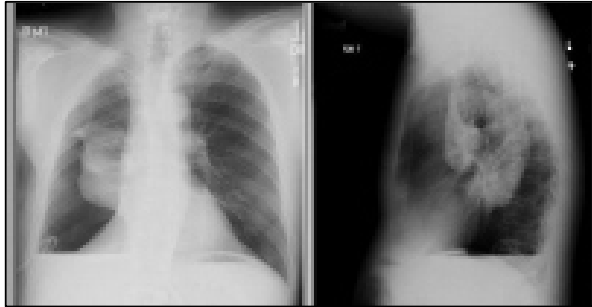
- Lung entrapment with malignant effusions is most common with mesothelioma or primary lung cancer.



Image5. Massive right pleural effusion with shift of mediastinum towards left

• Attempts at therapeutic thoracentesis usually do not improve dyspnea in patients with lung entrapment, due to the inability of the lung to reexpand. In fact, attempts at drainage of fluid in these patients usually results in a hydropneumothorax visualized on postprocedure imaging studies. Note the image 6.

Image 6.
Lung entrapment
with right
hydropneumothorax
and pleural drain in place



Tube thoracostomy. Although small, freely flowing parapneumonic effusions can be drained by therapeutic thoracentesis, most larger effusions and complicated parapneumonic effusions or empyemas require drainage by tube thoracostomy.

Traditionally, large-bore chest tubes (20-36F) have been used to drain thick pleural fluid and to break up loculations in empyemas. However, such tubes are not always well tolerated by patients and are difficult to direct correctly into the pleural space. More recently, small-bore tubes (7-14F) inserted at the bedside or under radiographic guidance have been shown to provide adequate drainage, even when empyema is present. These tubes cause less discomfort and are more likely to be placed successfully within a pocket of pleural fluid. Using 20-cm water suction and flushing the tube with normal saline every 6-8 hours may prevent occlusion of small-bore catheters.

Insertion of additional pleural catheters, usually under radiographic guidance, or instilling fibrinolytics (eg, streptokinase, urokinase, or alteplase) through the pleural catheter can help drain multiloculated pleural effusions

Pleurodesis or pleural sclerosis. Pleurodesis (also known as pleural sclerosis) involves instilling an irritant into the pleural space to cause inflammatory changes that result in bridging fibrosis between the visceral and parietal pleural surfaces, effectively obliterating the potential pleural space. Pleurodesis is most often used for recurrent malignant effusions, such as in patients with lung cancer or metastatic breast or ovarian cancer. Given the limited life expectancy of these patients, the goal of therapy is to palliate symptoms while minimizing patient discomfort, hospital length of stay, and overall costs.

Patients with poor performance status (Karnofsky score <70) and life expectancy of less than 3 months can be treated with repeated outpatient thora-

centesis as needed to palliate symptoms. Unfortunately, pleural effusions can reaccumulate rapidly, and the risk of complications increases with repeated drainage. In addition, patients with lung entrapment from malignant effusions are not candidates for repeated thoracentesis, which does not provide relief of dyspnea in such patients, nor for pleurodesis, as the visceral and parietal pleural surfaces cannot stay apposed to allow the bridging fibrosis. The best treatment for effusions in such patients is the insertion of an indwelling tunneled catheter, which allows patients to remove pleural fluid as needed at home.

Various agents, including talc, doxycycline, bleomycin sulfate (Blenoxane), zinc sulfate, and quinacrine hydrochloride can sclerose the pleural space and effectively prevent recurrence of the malignant pleural effusion.

Talc is the most effective sclerosing agent and can be administered as slurry through chest tubes or pleural catheters. Although a systematic review suggested that direct insufflation of talc via thoracoscopy was more effective than talc slurry, both were equally effective in a 2005 prospective trial of malignant effusions. Importantly, talc particles

- tend to occlude the small drainage holes in small pleural catheters. Therefore, pleural catheters should be at least 10-12F if intended for talc pleurodesis.

- Doxycycline and bleomycin are also effective in most patients and can be administered more easily through small-bore catheters, although they are somewhat less effective and substantially more expensive than talc.

- All sclerosing agents can produce fever, chest pain, and nausea.

- Talc rarely causes more serious adverse effects such as empyema and acute lung injury. The latter appears to be related to the particle size and amount of talc injected for pleurodesis.

- Injection of 50 mL of 1% lidocaine hydrochloride prior to instillation of the sclerosing agent might help alleviate pain. Additional analgesia might be required in some cases.

- Clamp chest tubes for approximately 2 hours after instillation of the sclerosing agent.

- A 2006 systematic review confirms that rotating the patient through different positions does not appear necessary to ensure distribution of soluble sclerosing agents throughout the pleural space. In addition, neither protracted drainage after instillation of sclerotics nor use of larger bore chest tubes increased the effectiveness of pleurodesis.

- Pleural sclerosis is likely to be successful only if the pleural space is drained completely before pleurodesis and if the lung is fully reexpanded to appose the visceral and parietal pleura after sclerosis. Animal studies suggest that systemic corticosteroids can reduce inflammation during sclerosis and can cause pleurodesis failures.

Depending on the results of the procedures, some diagnostic tests are sometimes performed: Computed tomography (CT) scan, Ultrasonography, Magnetic resonance imaging (MRI)

Treatment

Treatment has several goals:

- Remove the fluid, air, or blood from the pleural space.
- Relieve symptoms.
- Treat the underlying condition.

Medical Care

Transudative effusions are usually managed by treating the underlying medical disorder. However, whether transudates or exudates, refractory large pleural effusions causing severe respiratory symptoms, even if the cause is understood and disease-specific treatment is available, can be drained to provide relief. The management of exudative effusions depends on the underlying etiology of the effusion. Pneumonia, malignancy, or TB causes most diagnosed exudative pleural effusions, with the remainder typically deemed idiopathic. Complicated parapneumonic effusions and empyemas should be drained to prevent development of fibrosing pleuritis. Malignant effusions are usually drained to palliate symptoms and may require pleurodesis to prevent recurrence.

Medications cause only a small proportion of all pleural effusions and are associated with exudative pleural effusions. However, early recognition of these iatrogenic causes of pleural effusion avoids unnecessary additional diagnostic procedures and leads to definitive therapy, which is discontinuation of the medication. Implicated drugs include medications that cause drug-induced lupus syndrome (eg, procainamide, hydralazine, quinidine), nitrofurantoin, dantrolene, methysergide, procarbazine, and methotrexate.

Of the common causes for exudative pleural effusions, parapneumonic effusions have the highest diagnostic priority. Even in the face of antibiotic therapy, infected pleural effusions can rapidly coagulate and organize to form fibrous peels that might require surgical decortication. Therefore, quickly assess pleural fluid characteristics predictive of a complicated course to identify parapneumonic effusions that require urgent tube drainage, which are observed more commonly in indolent anaerobic pneumonias than in typical community-acquired pneumonia.

- Indications for urgent drainage of parapneumonic effusions include (1) frankly purulent fluid, (2) pleural fluid pH less than 7.2, (3) loculated effusions, and (4) bacteria on Gram stain or culture.

- Patients with parapneumonic effusions who do not meet criteria for immediate tube drainage should improve clinically within 1 week with appropriate antibiotic treatment.

- Reassess patients with parapneumonic effusions who do not improve or who deteriorate clinically using chest CT imaging to evaluate the pleural space and direct further drainage attempts, if needed.

Malignant pleural effusions usually signify incurable disease with considerable morbidity and a dismal mean survival of less than 1 year. For some patients, drainage of large malignant effusions relieves dyspnea caused by distortion of the diaphragm and chest wall produced by the effusion. Such effusions tend to recur, necessitating repeated thoracentesis, pleurodesis, or placement of indwelling tunneled catheters. Drainage systems using tunneled catheters (eg, PleurX, Denver Biomedicals, Denver, Colo; Aspira, Bard Access Systems, Salt Lake City, Utah) allow patients to drain their effusions as needed in the community.

For patients with lung entrapment from malignant effusions, such indwelling tunneled catheter drainage systems are the preferred treatment and provide good palliation of symptoms. In patients without lung entrapment, pleural sclerosis is another option to prevent recurrence of symptomatic effusions.

Tuberculosis (TB) pleuritis typically is self-limited. However, because 65% of patients with primary TB pleuritis reactivate their disease within 5 years, empiric anti-TB treatment is usually begun pending culture results when sufficient clinical suspicion is present, such as an unexplained exudative or lymphocytic effusion in a patient with a positive PPD finding. Chylous effusions are usually managed by dietary and surgical modalities discussed below. However, studies suggest that somatostatin analogues also may help in reducing efflux of chyle into the pleural space.

The following may be helpful in the management of pleurisy:

- Lying on the painful side may be more comfortable.
- Breathing deeply and coughing to clear mucus as the pain eases. Otherwise, pneumonia may develop.
- Getting rest.

Surgical Care. Surgical intervention is most often required for parapneumonic effusions that cannot be drained adequately by needle or small-bore catheters, and surgery might be required for diagnosis and sclerosis of exudative effusions.

- Video-assisted thoracoscopy with the patient under local or general anesthesia allows direct visualization and biopsy of the pleura for diagnosis of exudative effusions.

- Pleural sclerosis by insufflating talc directly onto the pleural surface using video-assisted thoracoscopy is an alternative to using talc slurries.

- Decortication is usually needed for trapped lungs to remove a thick, inelastic pleural peel that restricts ventilation and produces progressive or refractory dyspnea. In patients with chronic, organizing parapneumonic pleural

effusions, technically demanding operations might be required to drain loculated pleural fluid and to obliterate the pleural space.

- Surgically implanted pleuroperitoneal shunts are another treatment options for recurrent symptomatic effusions, most often in the setting of malignancy, but they are also used for management of chylous effusions. However, the shunts are prone to malfunction over time, are poorly tolerated by patients, and can require surgical revision.

In unusual cases, surgery might be required to close diaphragmatic defects (thereby preventing recurrent accumulation of pleural effusions

- in patients with ascites) and to ligate the thoracic duct to prevent reaccumulation of chylous effusions.

Consultations. A pulmonologist can be consulted for assistance with high-risk diagnostic thoracentesis, depending on the experience of the clinician. Drainage of complicated effusions usually requires consultation with a pulmonologist, interventional radiologist, or thoracic surgeon, depending on the location of the effusion and the clinical situation.

Diet. Restrictions of fat intake might help in the management of chylous effusions, although management remains controversial. Ongoing drainage of these effusions can rapidly deplete patients of fat and protein stores. Limiting oral fat intake might slow the accumulation of chylous effusions in some patients. Hyperalimentation or total parenteral nutrition can preserve nutritional stores and limit accumulation of the chylous effusion but probably should be restricted to patients in whom definitive therapy for the underlying cause of the chylous effusion is possible.

Further Inpatient Care

Monitoring pleural drainage. Record the amount and quality of fluid drained and monitor for an air leak (bubbling through the water seal) each shift. Large air leaks (steady streams of air throughout the respiratory cycle) may be indications of loose connectors or of a drainage port on the catheter that has migrated out to the skin. Alternatively, they may indicate large bronchopleural fistulae. Consequently, dressings should be taken down and the position of the catheter inspected at the puncture site. Briefly clamping the catheter at the skin helps determine whether the air leak is originating from within the pleural cavity (in which case it stops when the tube is clamped) or from outside the chest (in which case the leak persists).

Repeat the chest radiographs when drainage decreases to less than 100 mL/d to evaluate whether the effusion has been fully drained. If a large effusion persists radiographically, reevaluate the position of the chest catheter using chest CT scanning to ensure that the drainage ports are still positioned within the pleural collection. If the catheter is positioned appropriately, consider in-

jecting lytics through the chest tube to break up clots that may be obstructing drainage. Alternatively, chest CT imaging may reveal lung entrapment/trapped lung, which is unlikely to respond to further drainage in the hospital.

Medicolegal Pitfalls

- Failure to recognize potentially lethal underlying conditions producing pleural effusions, including pulmonary embolus and esophageal rupture
- Discharge or transfer of a patient with an unrecognized pneumothorax following thoracentesis
- Failure to prevent constrictive pleuritis from untreated parapneumonic effusions or hemothorax
- Unnecessary attempt to perform thoracentesis

Prognosis

Prognosis varies in accordance with the underlying etiology.

- Malignant effusions convey a very poor prognosis, with median survival of 4 months and mean survival less than 1 year. Effusions from cancers that are more responsive to chemotherapy, such as lymphoma or breast cancer, are more likely to be associated with prolonged survival compared with those from lung cancer or mesothelioma.
- Parapneumonic effusions, when recognized and treated promptly, typically resolve without significant sequelae. However, untreated or inappropriately treated parapneumonic effusions may lead to constrictive fibrosis.

LIST OF SUGGESTED READING

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Навчальне видання

**Модуль 3. Сучасна практика внутрішньої медицини.
Змістовний модуль №4.
Введення хворих у пульмонологічній клініці.
Тема 6. Ведення хворих
з плевральним випотом**

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Комп'ютерний набір
Немцова В.Д.

План 2012, поз. 28.

Підп. до друку 12.06.2012. Формат А5. Папір типогр. Різографія.
Умов. друк. арк. 1,5. Тираж 150 прим. Зам. № 12-2931.

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Свідоцтво про внесення суб'єкта видавничої справи до Державного реєстру видавництв, виготовників і розповсюджувачів видавничої продукції серії ДК № 3242 від 18.07.2008 р.

**Modul 3. Current practice of internal medicine.
Meaningful module №4.
Keeping patients in pulmonological clinic.
Theme 6. Management of patients
with pleural effusion**

Guidelines for students and interns



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