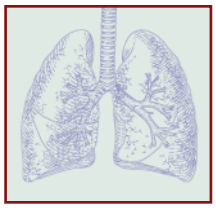

Diagnosis of Pleural Effusion: A Systematic Approach

By Emmet E. McGrath, MB, PhD, MRCPI, and Paul B. Anderson, MA, FRCP

CE 1.0 Hour

Notice to CE enrollees:

A closed-book, multiple-choice examination following this article tests your understanding of the following objectives:

1. Identify 3 characteristics of abnormal pleural fluid.
2. Describe a systematic algorithm for the investigation of pleural effusions.
3. Differentiate between extudates and transdates.

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In most diseases related to pleural effusion, the fluid analysis yields important diagnostic information, and in certain cases, fluid analysis alone is enough for diagnosis. The many important characteristics of pleural fluid are described, as are other complementary investigations that can assist with the diagnosis of common and rare pleural effusions. For a systematic review of pleural effusion, a literature search for articles on the practical investigation and diagnosis of pleural effusion was done. Articles included guidelines, expert opinion, experimental and nonexperimental studies, literature reviews, and systematic reviews published from May 2003 through June 2009. The search yielded 1 guideline, 2 meta-analyses, 9 literature reviews, 1 randomized control trial, and 9 clinical studies. On the basis of class IIa or class I evidence from these articles, a step by step approach is recommended for investigating a pleural effusion, beginning with assessment of the medical history, clinical examination, radiology, pleural fluid evaluation, and finally, if no diagnosis is forthcoming, a pleural biopsy under image guidance or thoracoscopy. (*American Journal of Critical Care.* 2011;20:119-128)

In a normal pleural space, fluid enters and exits at a constant, equal rate because of the ongoing filtration of a small amount of low-protein liquid in normal microvessels. Near the end of the 19th century, Starling and Tubby[1] hypothesized that the exchange of microvascular fluid and solutes was governed by the balance between hydrostatic pressure, osmotic pressure, and membrane permeability, and they devised the Starling equation:

$$Q_F = L_P \times A[(P_{CAP} - P_{PL}) - \zeta_D(pi_{CAP} - pi_{PL})]$$

where Q_F is fluid movement, L_P is the filtration coefficient, A is the surface area of the pleura, ζ_D is the reflection coefficient for protein movement across the pleura (PL), P is the hydrostatic pressure of the pulmonary capillary bed (CAP), and pi is the oncotic pressure of pleural space.[1,2] This equation formed the basis for understanding fluid accumulation in the pleural space, where the hydrostatic forces that filter water out of the vessel are balanced by osmotic forces that reabsorb water back into the vessel. In the pleura, reabsorption is facilitated by the extensive lymphatic system on the diaphragm and mediastinal surfaces of the parietal pleura.[2]

Fluid accumulation in the pleural space indicates disease. The accumulation is associated with many medical conditions that predispose to fluid accumulation via many different mechanisms, including increased pulmonary capillary pressure, decreased oncotic pressure, increased pleural membrane permeability, and obstruction of lymphatic flow.[3]

The most common conditions causing effusions are cardiac failure, pneumonia, and malignant neoplasm.

The most common conditions that result in effusions are cardiac failure, pneumonia, and malignant neoplasm. Diagnosis of a pleural effusion begins with obtaining the patient's clinical history and doing a physical examination and is followed by chest radiography and analysis of pleural fluid in appropriate instances. If necessary, the process continues with further investigative studies, such as computed tomography (CT) of the thorax, pleural biopsy, thoracoscopy, and, occasionally, bronchoscopy.

Methods

Articles used for this review were selected by using MEDLINE to search for English-language articles on pleural effusion published from May 2003 through June 2009. In addition, hand searching of the bibliographies of retrieved articles was done by recognized world authorities on pleural effusions. Keywords used for the search were *pleural effusion, investigation,* and *diagnosis.* All types of evidence (guidelines, expert opinion, experimental and nonexperimental studies, literature reviews, and systematic reviews) in English were examined, but only material that involved the practical and clinical investigation and diagnosis of pleural effusion in adults was included in the final review. Case reports were excluded. Important articles by world leading experts cited in articles from the search were also reviewed.

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Results

Although many articles have been written on pleural effusion, the number included in our review was markedly reduced when only English-language publications about the clinical and practical investigation and diagnosis of this abnormality were sought by using the key words *investigation* and *diagnosis* together. The number was also reduced further when case reports were excluded. From May 2003 through June 2009, a total of 1 guideline,[3] 2 meta-analyses,[4,5] 9 literature reviews,[6-14] 1 randomized controlled trial,[15] and 9 clinical studies[16-24] on the practical investigation and diagnosis of pleural effusion were published in peer-reviewed journals.

Evidence was assessed as class I, class IIa, class IIb, indeterminate, and class III.[25] Class I evidence is definite recommendation of a practice that is based on the results of at least 1 randomized controlled trial and is considered a definitive standard of care or best practice. Good evidence and expert opinion are considered class II. Fair to good evidence is classified as class IIb. A finding of no benefit or harm

is considered indeterminate; usually evidence is classified as indeterminate because it is insufficient (eg, evidence provided by preliminary data). Class III evidence is evidence that is not useful and may be harmful.

Clinical Features of Pleural Effusions

The clinical history and physical examination can be quite helpful in indicating appropriate investigation. Patients with pleural effusions usually have dyspnea, cough, and occasional sharp nonradiating chest pain that is often pleuritic. A history of cardiac, renal, or liver impairment can suggest a transudative effusion. A history of cancer can be suggestive of a malignant pleural effusion. Recent leg swelling or deep-vein thrombosis may result in an effusion related to pulmonary embolism.[6] A history of recent or current pneumonia suggests a parapneumonic effusion, either complicated (empyema) or uncomplicated. Previous trauma may result in hemothorax or chylothorax. Previous exposure to asbestos is common in patients who have a benign effusion related to the exposure or have mesothelioma.[6] Recent esophageal dilatation or endoscopy can result in esophageal rupture. Certain medications, including amiodarone, methotrexate, phenytoin, and nitrofurantoin, can cause pleural effusions.[3] Rheumatoid arthritis and other autoimmune conditions can also result in effusions.

A sign such as hemoptysis may be associated with a malignant neoplasm, pulmonary embolism, or severe tuberculosis. Fever occurs in tuberculosis, empyema, and pneumonia. Weight loss can be associated with a malignant neoplasm and tuberculosis.

Physical findings such as ascites may indicate cirrhosis, ovarian cancer, or Meig syndrome.[6] Unilateral leg swelling can strongly indicate pulmonary embolism, and bilateral leg swelling is associated with transudates such as those caused by heart or liver failure. A pericardial friction rub occurs in pericarditis. In general, the clinician moves from suspecting effusion on the basis of clinical history and examination to proving an effusion exists by means of chest radiography before fluid sampling is considered.

For a unilateral pleural effusion evident on chest radiographs, the differential diagnosis is extensive (Table 1). The differential diagnosis for bilateral pleural effusions is narrower and includes causes of transudative effusions, such as cardiac, hepatic, and renal failure and hypoalbuminemia, and in rare cases, malignant neoplasm, pulmonary embolism, and rheumatoid arthritis. Congestive heart failure is the most common cause of bilateral pleural effusion, and in patients with clinical or radiological evidence of congestive heart failure, investigation of the effusion need not go any further.[3] Diagnostic thoracentesis is required only if a patient has bilateral effusions that are unequal in size, has an effusion that does not respond to therapy, has pleuritic chest pain, or is febrile.[6] The effusions usually improve quite quickly once diuretic therapy is started.

Table 1
Causes of transudative and exudative unilateral effusion[a]

Type	Exudate	Transudate
Common		
	Parapneumonic effusions	Left ventricular failure
	Malignant neoplasm	Cirrhotic liver disease Hypoalbuminemia Peritoneal dialysis
Less common		
	Pulmonary embolism	Nephrotic syndrome
	Rheumatoid arthritis	Pulmonary embolism
	Benign effusion associated with exposure to asbestos	Hypothyroidism
	Pancreatitis	Mitral stenosis
	After myocardial infarction syndrome	
	Autoimmune diseases	
	After coronary artery bypass surgery	
Rare		
	Subphrenic, hepatic, or splenic abscess	Constrictive pericarditis
	Uremia	Meig syndrome
	Chylothorax	Urinothorax
	Other infections	Superior vena cava obstruction
	Drug induced	Ovarian hyperstimulation
	Radiotherapy	
	Esophageal rupture	

[a]Based on data from Maskell et al.[3]

Symptoms include dyspnea, cough, and occasionally sharp, nonradiating, pleuritic chest pain.

Diagnostic Thoracentesis

Thoracentesis with analysis of the fluid can quickly narrow the differential diagnosis of an effusion. Most aspirates consist of a straw-yellow fluid; this finding is nonspecific because it occurs in many types of pleural effusion. However, other appearances can be helpful (Table 2). The fluid may be bloodstained in conditions such as pneumonia, malignant neoplasm, pulmonary

Table 2
Relationship between pleural fluid appearance and causes[a]

Cause	Fluid appearance/odor
Pseudochylothorax and chylothorax	Milky white
Urinothorax	Urine
Anaerobic empyema	Putrid
Chylothorax	Bile stained
Aspergillus infection	Black
Empyema	Turbid
Amebic liver abscess	"Anchovy" brown
Esophageal rupture	Food particles
Trauma, pulmonary embolism, benign asbestos-related effusion, pneumonia, malignant neoplasm, after myocardial infarction syndrome	Bloodstained

[a]Based on data from Maskell et al.[3]

Figure 1 Milky pleural aspirate.

Table 3
Light's criteria for distinguishing between pleural exudates and transudates

Fluid is an exudate if 1 *or more of the following criteria are met*

1. Ratio of pleural fluid level of lactate dehydrogenase (LDH) to serum level of LDH is greater than 0.6
2. Pleural fluid level of LDH is more than two-thirds the upper limit of the reference range for the serum level of LDH
3. Ratio of pleural fluid level of protein to serum level of protein is greater than 0.5

embolism with infarction, benign effusion related to asbestos exposure, and trauma.[19] In frankly bloody effusions, a fluid hematocrit level greater than half the serum hematocrit level is indicative of hemothorax.[3] If the fluid is particularly turbid or milky (Figure 1), centrifugation is useful in differentiating empyema from chylothorax or pseudochylothorax. In empyema, the supernatant fluid is clear where the cell debris forms a pellet. In chylothorax or pseudochylothorax, the fluid remains uniform due to the high lipid content.[3] Anchovy-brown fluid and black fluid are indicative of amebic liver abscess and *Aspergillus* infection, respectively.

Once aspirated, the fluid is sent for biochemical, microbiological, and cytological analyses. Biochemical analyses include determination of protein, pH, lactic dehydrogenase, glucose, and albumin levels. Because it enters the pleural space with water, protein has become an important marker in the differentiation of transudates from exudates.

A pleural effusion with a protein level less than 30 g/L indicates a transudate, whereas one with a level greater than 30 g/L indicates an exudate, provided the serum protein level is within the normal reference range. When a protein level greater than 30 g/L is used as the only basis for determining the type of effusion, 10% of exudates and 15% of transudates are misclassified.[26] Consequently, the use of Light's criteria (Table 3) is recommended when the protein level is between 25 and 35 g/L.[27] Use of these criteria requires the additional measurement of a patient's serum levels of lactic dehydrogenase and protein. Although Light's criteria are almost 100% sensitive for exudates, in a prospective comparative study of pleural effusions in 172 patients, Porcel et al[28] found that approximately 20% of the patients with heart failure who were taking diuretics also met Light's criteria for an exudate. In such instances, if the difference between serum and pleural levels of protein is greater than 31 g/L, the effusion should be classified as a transudate.[29] Albumin levels can also be used in this manner: a difference of more than 12 g/L between serum and fluid levels indicates a transudate.[30] Of note, a large percentage of exudates will be misclassified if these gradients are used as the only method of differentiating between transudates and exudates.[6]

A pH less than 7.2 in infected effusions indicates a complicated parapneumonic effusion (empyema) until proved otherwise, and insertion of chest drain and fluid removal are priorities.[3,6] A low pH can also occur in esophageal rupture, rheumatoid arthritis, and malignant neoplasm associated with poor outcome.[6] Elevated levels of lactate dehydrogenase occur in lymphoma and tuberculosis; levels greater than 1000 U/L (to convert units per liter to microkatals per liter, multiply by 0.0167) are associated with empyema.[6] In an exudative effusion, pleural glucose

levels less than 28.8 mg/dL (to convert milligrams per deciliter to millimoles per liter, multiply by 0.0555) occur in tuberculosis, malignant neoplasm, empyema, rheumatoid arthritis, systemic lupus erythematosus, and esophageal rupture. Rheumatoid arthritis probably is not responsible for a pleural effusion if the fluid glucose level is greater than 1.6 mmol/L.[3] Cell differential analysis can also help narrow the differential diagnosis. Fluid lymphocytosis occurs in conditions such as tuberculosis, sarcoidosis, chylothorax, rheumatoid arthritis, and malignant neoplasm, including lymphoma.[30,31]

Pleural fluid predominated by neutrophils is associated with pulmonary embolism, parapneumonic effusion, acute tuberculosis, and benign effusion related to exposure to asbestos.[31]

A predominance of eosinophils in pleural fluid has no diagnostic value, and up to one-third of this type of effusion is never diagnosed.[32] However, effusions with mostly eosinophils have been associated with air or blood in the pleural space.[6]

Routine microbiological analysis includes sending a fluid sample for Gram and Ziehl-Neelson stains and cultures to detect mycobacteria and other bacteria.

Cytological analysis is extremely important if a malignant neoplasm is suspected, and the analyses are positive for a malignant tumor in 60% of patients who have such a neoplasm.[3] If the first sample is negative for tumor, sending a second sample is worthwhile because analysis of 2 samples markedly increases the chance of diagnosis of malignant neoplasm.[33]

Levels of adenosine deaminase (ADA) levels are particularly useful in areas where the prevalence of tuberculosis is high. An ADA level greater than 40 U/L (to convert units per liter to nanokatals per liter, multiply by 16.667) has a sensitivity of more than 90% and a specificity of about 85% for the presence of tuberculosis.[4,34] In lymphocyte-predominant effusions, the specificity of ADA for tuberculosis increases to more than 95%. Elevated ADA also occurs with malignant neoplasm, empyema, and rheumatoid arthritis.[35] Of note, ADA levels may be normal in the pleural fluid of patients positive for human immunodeficiency virus who have tuberculosis.[36]

Several more unusual tests of pleural fluid can be performed if clinical findings indicate[3,6] (Table 4). The results may be helpful in making the relevant diagnosis. In particular, polymerase chain reaction, tumor markers, and complement are currently of much interest. Polymerase chain reaction is useful in diagnosing *Streptococcus pneumoniae* infection and tuberculosis. For tuberculosis, the sensitivity is 40% to 60% and the specificity is greater than 90%, although the last percentage is reduced in patients who have cultures negative for mycobacteria.[6,37]

Table 4
Useful further tests of pleural fluid for assessing the causes of pleural effusion[a]

Test	Suggested diagnosis
Cholesterol level Triglyceride level	Chylothorax or pseudochylothorax (see Table 5)
Hematocrit level	Hemothorax if >50% serum hematocrit level
Amylase level	Pancreatitis or esophageal rupture, depending on isotype
NT-proBNP level	Heart failure, if elevated
Creatinine level	Urinothorax if pleural fluid creatinine >serum creatinine
Polymerase chain reaction	Tuberculosis or *Streptococcus pneumoniae* infection
Tumor markers CEA, CA 15.3, CA 549 levels	Breast carcinoma
CYFRA 21-1 level	Lung carcinoma
CA 125, HER-2/neu level	Ovarian, endometrial, and breast cancers
Complement C4 level	Rheumatoid arthritis, if reduced
Centrifugation	Used to differentiate empyema from chylothorax or pseudochylothorax

Abbreviations: CA, cancer antigen; CEA, carcinoembryonic antigen; CYFRA, cytokeratin-19 fragments; HER, human epidermal growth receptor; NT-proBNP, N-terminal pro B-type natriuretic peptide.

[a]Based on data from Porcel and Light.[6]

Table 5
Pleural fluid characteristics of chylothorax and pseudochylothorax

Results of fluid analysis	Pseudochylothorax	Chylothorax
Triglyceride level, mmol/L (mg/dL)	<0.56 (50)	>1.24 (110)
Cholesterol level, mmol/L (mg/dL)	>5.18 (200)	<5.18 (200)
Cholesterol crystals	Yes, common	No
Chylomicrons	No	Yes

Tumor markers in pleural fluid may be useful in certain clinical situations, although in general the sensitivity is quite low (<30%) when high specificity is required.[6] Use of a combination of different tumor markers may increase sensitivity, and the results should be interpreted in combination with clinical findings and the results of conventional tests.[16] In a prospective study of 224 patients with confirmed pleural malignant neoplasm, Bielsa et al[17] found that tumor markers in the pleural fluid could be useful in predicting survival. In patients with adenocarcinomatous or squamous malignant effusion, the combination of pleural fluid levels of 1000 U/mL or greater for cancer antigen 125 and 100 ng/mL or

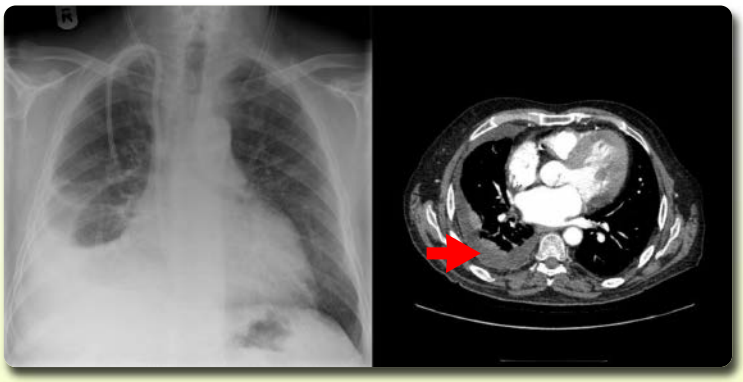

Figure 2 Chest radiograph and computed tomography scan of thorax show a right-sided effusion (arrow).

greater for cytokeratin-19 fragments 21-1 was predictive of a lower survival (4 vs 11.7 months for adenocarcinoma, 0.3 vs 8.4 months for squamous cell carcinoma). This tumor marker combination remained an independent predictor of poor outcome after adjustments were made for age and tumor type.[17]

In frankly bloody effusions, a fluid hematocrit of more than half the serum hematocrit indicates hemothorax.

Complement levels in pleural fluid have traditionally been analyzed when autoimmune disease such as rheumatoid arthritis or systemic lupus erythematosus is suspected (reduced levels of complement). However, recently an association between transudates and low complement levels was described. In a prospective study of 135 patients with pleural effusion of known causes (cardiac failure, malignant neoplasm, parapneumonia, after lung transplant, and Dressler syndrome), Shitrit et al[18] found that effusions related to congestive heart failure could be differentiated from parapneumonic and postoperative pleural effusions by the low level of complement in the first type. Normal levels of complement almost unequivocally indicate that congestive heart failure is not an etiological factor. Shitrit et al[18] also noted that in lung transplant recipients, normal or high levels of complement in pleural fluid may indicate that the pleural effusion is not attributable to the surgery, but to another secondary cause (eg, parapneumonic effusions).

Removal of all the fluid before the computed tomography is done will result in less than optimal imaging.

A conventional posteroanterior radiograph can show the presence of an effusion (Figure 2). Lateral chest radiographs can be used to detect small effusions. If any doubt exists, thoracic ultrasound is useful in detecting small effusions, differentiating pleural fluid from pleural thickening, and aspirating fluid from especially small or loculated effusions. Thoracic CT with contrast material can show pathological pulmonary changes such as pneumonia or tumor and pleural thickening and nodularity that may be amenable to percutaneous biopsy. An important step is to avoid draining all the fluid before CT is done because removal of all fluid results in less than optimal pleural imaging. If the clinical history and findings are suggestive of pulmonary embolism, then helical CT may be indicated.[3]

If the results of fluid analysis and radiology are not sufficient for diagnosing a persistent unexplained exudative effusion, then a pleural biopsy is indicated. The biopsy may be blind, image guided, or thoracoscopic. As shown in a retrospective analysis of the diagnosis of pleural effusions in 414 patients by Prakash and Reiman,[38] blind closed biopsy has traditionally been of little benefit in diagnosing malignant effusions in patients whose cytological assays showed no malignant cells. Indeed, fluid cytology is superior to blind closed pleural biopsy in the diagnosis of malignant disease.[6] Poe et al[39] retrospectively analyzed 211 patients who underwent pleural biopsy during a 6-year period and found that blind closed pleural biopsy was useful in diagnosing tuberculosis, especially in patients with fluid lymphocytosis. In these patients, the diagnostic rate was greater than 90% when tissue was analyzed both histologically and microbiologically. In a small but important study of 50 consecutive patients with suspected pleural malignant disease whose cytological assays showed no malignant cells, Maskell et al[15] found that image-guided pleural biopsy greatly assisted in the diagnosis of malignant neoplasm and was better than blind closed biopsy. Consequently, image-guided biopsy has essentially replaced the blind biopsy technique. With image guidance, areas of pleural thickening or nodularity can be accurately biopsied, thus increasing the diagnostic rate.[15]

Image-guided biopsy is also useful in patients who are too weak to undergo thoracoscopy. In patients with no evidence of malignant disease, pleural thickening, or pleural nodularity, or if the results of image-guided biopsy are negative for malignant disease, thoracoscopy is indicated.[3] This technique allows close visual examination of the pleura and accurate biopsy of abnormal tissue and is diagnostic in approximately 90% of cases. Thoracoscopy can be performed by either a pulmonologist (medical thoracoscopy) or a surgeon (video-assisted thoracoscopic surgery). Drainage of fluid and pleurodesis can be performed at the same time as the thoracoscopy if indicated, and in many medical facilities,

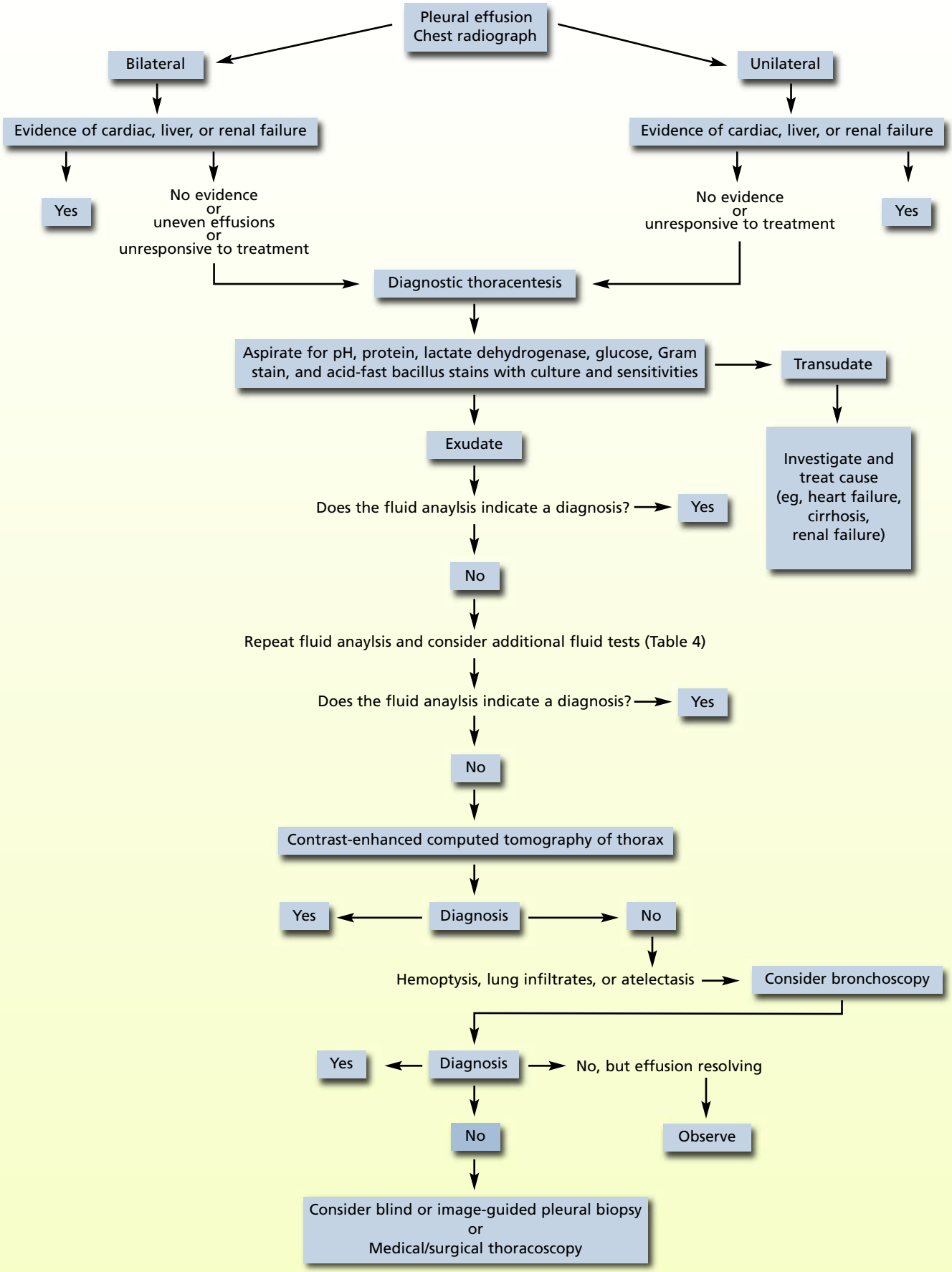

Figure 3 Recommended algorithm for investigation of a pleural effusion.

thoracoscopy is the next step for patients whose cytological results are negative for malignant cells.

Bronchoscopy is not routinely recommended in the investigation of pleural effusion unless the patient has hemoptysis or radiological features of malignant neoplasm such as a mass, massive pleural effusion, or a shift in the midline toward the side of the effusion.[6] In patients with massive effusion, drainage before bronchoscopy is recommended to allow an adequate examination without extrinsic compression.[3]

Recommendations Based on Current Evidence

Investigation of a pleural effusion evident on chest radiographs should follow a stepwise approach (Figure 3) to diagnosis. Diagnosis begins with the clinical history, physical examination, and chest radiography and is followed by thoracentesis when appropriate. The majority of the recommendations in Figure 3 represent class IIa evidence. An exception is the use of image-guided pleural biopsy (instead of blind pleural biopsy) in the last step of the algorithm; this type of biopsy has been assessed by using a randomized controlled trial and therefore represents class I evidence.

Examination of the pleural fluid can narrow the differential diagnosis considerably. The appearance of the fluid and biochemical parameters can be key to a direct diagnosis or can indicate the next step. In transudative effusions, the underlying cause should be sought and treated. In exudative effusions in which fluid analysis does not lead to immediate diagnosis, CT of the thorax should be performed. If the diagnosis is still not evident after CT, pleural biopsy (radiologically or medical thoracoscopy) is recommended. In a few patients, the effusion may begin to improve. In these instances, the patient should be observed; the disease process may be resolving and further invasive investigation may not be warranted.

FINANCIAL DISCLOSURES
None reported.

REFERENCES

1. Starling EH, Tubby A. On absorption from and secretion into the serous cavities. *J Physiol.* 1894;16:140-155.
2. Mitrouska I, Bouros D. The trans-exudative pleural effusion. *Chest.* 2002;122(5):1503-1505.
3. Maskell NA, Butland RJ; Pleural Diseases Group, Standards of Care Committee, British Thoracic Society. BTS guidelines for the investigation of a unilateral pleural effusion in adults. *Thorax.* 2003;58(suppl 2):ii8-ii17.
4. Morisson P, Neves DD. Evaluation of adenosine deaminase in the diagnosis of pleural tuberculosis: a Brazilian meta-analysis. *J Bras Pneumol.* 2008;34(4):217-224.
5. Goto M, Noguchi Y, Koyama H, Hira K, Shimbo T, Fukui T. Diagnostic value of adenosine deaminase in tuberculous pleural effusion: a meta-analysis. *Ann Clin Biochem.* 2003; 40(pt 4):374-381.
6. Porcel JM, Light RW. Diagnostic approach to pleural effusion in adults. *Am Fam Physician.* 2006;73(7):1211-1220.
7. Chapman SJ, Cookson WO, Musk AW, Lee YC. Benign asbestos pleural diseases. *Curr Opin Pulm Med.* 2003;9(4):266-271.
8. Romero-Candeira S, Hernández L. The separation of transudates and exudates with particular reference to the protein gradient. *Curr Opin Pulm Med.* 2004;10(4):294-298.
9. Kalomenidis I, Light RW. Pathogenesis of the eosinophilic pleural effusions. *Curr Opin Pulm Med.* 2004;10(4):289-293.
10. Medford A, Maskell N. Pleural effusion. *Postgrad Med J.* 2005;81(961):702-710.
11. Froudarakis ME. Diagnostic work-up of pleural effusions. *Respiration.* 2008;75(1):4-13.
12. Rahman NM, Munavvar M. Investigation of the patient with pleural effusion. *Clin Med.* 2009;9(2):174-178.
13. Rahman NM, Chapman SJ, Davies RJ. Pleural effusion: a structured approach to care. *Br Med Bull.* 2005;72:31-47.
14. Antony VB, Loddenkemper R, Astoul P, et al. Management of malignant pleural effusions. *Eur Respir J.* 2001;18(2):402-419.
15. Maskell NA, Gleeson FV, Davies RJ. Standard pleural biopsy versus CT-guided cutting-needle biopsy for diagnosis of malignant disease in pleural effusions: a randomised controlled trial. *Lancet.* 2003;361(9366):1326-1330.
16. Liang QL, Shi HZ, Qin XJ, Liang XD, Jiang J, Yang HB. Diagnostic accuracy of tumor markers for malignant pleural effusion: a meta-analysis. *Thorax.* 2008;63(1):35-41.
17. Bielsa S, Esquerda A, Salud A, et al. High levels of tumor markers in pleural fluid correlate with poor survival in patients with adenocarcinomatous or squamous malignant effusions. *Eur J Intern Med.* 2009;20(4):383-386.
18. Shitrit D, Ollech JE, Ollech A, et al. Diagnostic value of complement components in pleural fluid: report of 135 cases. *Respir Med.* 2008;102(11):1631-1635.
19. Villena V, López-Encuentra A, García-Luján R, Echave-Sustaeta J, Martínez CJ. Clinical implications of appearance of pleural fluid at thoracentesis. *Chest.* 2004;125(1):156-159.
20. Gao ZC, Tian RX. Clinical investigation on diagnostic value of interferon-gamma, interleukin-12 and adenosine deaminase isoenzyme for tuberculous pleurisy. *Chin Med J (Engl).* 2005;118(3):234-237.
21. Chakrabarti B, Ryland I, Sheard J, Warburton CJ, Earis JE. The role of Abrams percutaneous pleural biopsy in the investigation of exudative pleural effusions. *Chest.* 2006; 129(6):1549-1555.
22. Jiménez D, Díaz G, García-Rull S, Vidal R, Sueiro A, Light RW. Routine use of pleural fluid cultures: are they indicated? Limited yield, minimal impact on treatment decisions. *Respir Med.* 2006;100(11):2048-2052
23. Qureshi NR, Rahman NM, Gleeson FV. Thoracic ultrasound in the diagnosis of malignant pleural effusion. *Thorax.* 2009;64(2):139-143.
24. Yap E, Anderson G, Donald J, Wong CA, Lee YC, Sivakumaran P. Pleural effusion in patients with pulmonary embolism. *Respirology.* 2008;13(6):832-836.
25. ECC guidelines: part 1: introduction to the international guidelines 2000 for CPR and ECC. *Circulation.* 2000; 102(suppl 1):I-1-I-11.
26. Sahn SA, Heffner JE. Pleural fluid analysis. In: Light RW, Gary Lee YC. *Textbook of Pleural Diseases.* London, England: Arnold; 2003:191-209.
27. Light RW. Pleural effusion. *N Engl J Med.* 2002;346(25): 1971-1977.
28. Porcel JM, Vives M, Vicente de Vera MC, Cao G, Rubio M, Rivas MC. Useful tests on pleural fluid that distinguish transudates from exudates. *Ann Clin Biochem.* 2001;38(pt 6):671-675.
29. Ansari T, Idell S. Management of undiagnosed persistent pleural effusions. *Clin Chest Med.* 1998;19(2):407-417.
30. Romero-Candeira S, Fernández C, Martín C, Sánchez-Paya J, Hernández L. Influence of diuretics on the concentration of proteins and other components of pleural transudates in patients with heart failure. *Am J Med.* 2001;110(9):681-686.

31. Light RW, Erozan YS, Ball WC Jr. Cells in pleural fluid: their value in differential diagnosis. *Arch Intern Med.* 1973;132(6):854-860.
32. Light RW. *Pleural Diseases.* 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2001.
33. Garcia LW, Ducatman BS, Wang HH. The value of multiple fluid specimens in the cytological diagnosis of malignancy. *Mod Pathol.* 1994;7(6):665-668.
34. Porcel JM, Vives M. Differentiating tuberculous from malignant pleural effusions: a scoring model. *Med Sci Monit.* 2003;9:CR175-CR180.
35. Burgess LJ, Maritz FJ, Le Roux I, Taljaard JJ. Use of adenosine deaminase as a diagnostic tool for tuberculous pleurisy. *Thorax.* 1995;50(6):672-674.
36. Hsu WH, Chiang CD, Huang PL. Diagnostic value of pleural adenosine deaminase in tuberculous effusions of immunocompromised hosts. *J Formos Med Assoc.* 1993;92(7):668-670.
37. Pai M, Flores LL, Hubbard A, Riley LW, Colford JM Jr. Nucleic acid amplification tests in the diagnosis of tuberculous pleuritis: a systematic review and meta-analysis. *BMC Infect Dis.* 2004;4:6.
38. Prakash UB, Reiman HM. Comparison of needle biopsy with cytologic analysis for the evaluation of pleural effusion: analysis of 414 cases. *Mayo Clin Proc.* 1985;60(3):158-164.
39. Poe RH, Israel RH, Utell MJ, Hall WJ, Greenblatt DW, Kallay MC. Sensitivity, specificity, and predictive values of closed pleural biopsy. *Arch Intern Med.* 1984;144(2):325-328.

CE Test Test ID A112002: Diagnosis of Pleural Effusion: A Systematic Approach.

Learning objectives: 1. Identify 3 characteristics of abnormal pleural fluid. 2. Describe a systematic algorithm for the investigation of pleural effusions. 3. Differentiate between extudates and transdates.

1. If a recommended practice is supported by only 1 randomized control study and a few case studies, it is considered to be which of the following?
a. Class I evidence
b. Class IIa evidence
c. Class IIb evidence
d. Class II evidence

2. A patient who was a construction worker in the 1950s has dyspnea, a cough, and sharp radiating chest pain. Which of the following is most likely to be the source of his pleural effusion?
a. Pneumonia
b. Mesothelioma
c. Pulmonary embolism
d. Rheumatoid arthritis

3. The patient with a pleural effusion caused by a pulmonary embolism is likely to have which of the following?
a. A pericardial friction rub
b. Bilateral leg swelling
c. Unilateral leg swelling
d. Weight loss

4. Which of the following is associated with blood stained pleural fluid?
a. *Aspergillus* infection
b. Amebic liver abscess
c. Pulmonary embolism
d. Pseudochylothorax

5. Why is it important to compare serum protein levels to pleural fluid protein levels when differentiating between an exudate and a transudate?
a. Normal serum protein with normal pleural protein signifies a transudate.
b. Normal serum protein with a pleural fluid less than a 30 g/L signifies an exudate.
c. If the difference between serum and pleural protein levels is 12 g/L or less, the effusion is classified as a transudate.
d. If the difference between serum and pleural protein levels is greater than 31 g/L, the effusion is classified as a transudate.

6. If a nurse is caring for a pneumonia patient undergoing a thoracentesis and the pleural fluid has a pH of 7.1, which of the following actions should the nurse take?
a. Schedule the patient for a computed tomography scan
b. Assist with chest tube insertion
c. Repeat the pleural fluid analysis
d. Schedule the patient for a bronchoscopy

7. Pleural fluid that has an elevated lactate dehydrogenase level is probably due to which of the following?
a. Rheumatoid arthritis
b. Tuberculosis
c. Systemic lupus erythematosus
d. Sarcoidosis

8. According to the algorithm, which of the following is the first step in the investigation of a pleural fluid following history and chest radiograph?
a. Computed tomography scan
b. Bronchoscopy
c. Thoracentesis
d. Pleural biopsy

9. A patient with congestive heart failure and a pleural effusion will most likely have which of the following?
a. Normal complement levels
b. Reduced complement levels
c. Elevated complement levels
d. No complement will be measured

10. Which of the following diagnostic tests would be most beneficial in diagnosing malignant disease after inconclusive radiology and fluid analysis?
a. Bronchoscopy
b. Image guided biopsy
c. Closed biopsy
d. Thoroscopy

11. Food particles in the pleural fluid can be a sign of which of the following?
a. Chylothorax
b. Trauma
c. Esophageal rupture
d. Anerobic empyema

12. Which of the following can cause a pleural effusion with unilateral exudates?
a. Malignant neoplasm
b. Cirrhotic liver disease
c. Hypothyroidism
d. Mitral stenosis

13. Pseudochylothorax can be differentiated from chylothorax if it contains which of the following?
a. Chylomicrons
b. Cholesterol crystals
c. Triglycerides 1.32
d. Cholesterol 4.2

Test ID: A112002 Contact hours: 1.0 Form expires: March 1, 2013. **Test Answers:** Mark only one box for your answer to each question. You may photocopy this form.

1.	2.	3.	4.	5.	6.	7.	8.	9.	10.	11.	12.	13.
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