Pleurisy

SARA M. KASS, CDR, MC, USN, PAMELA M. WILLIAMS, MAJ, USAF, MC, and
BRIAN V. REAMY, COL, USAF, MC, *Uniformed Services University of the Health Sciences, Bethesda, Maryland*

Pleuritic chest pain is a common presenting symptom and has many causes, which range from life-threatening to benign, self-limited conditions. Pulmonary embolism is the most common potentially life-threatening cause, found in 5 to 20 percent of patients who present to the emergency department with pleuritic pain. Other clinically significant conditions that may cause pleuritic pain include pericarditis, pneumonia, myocardial infarction, and pneumothorax. Patients should be evaluated appropriately for these conditions before an alternative diagnosis is made. History, physical examination, and chest radiography are recommended for all patients with pleuritic chest pain. Electrocardiography is helpful, especially if there is clinical suspicion of myocardial infarction, pulmonary embolism, or pericarditis. When these other significant causes of pleuritic pain have been excluded, the diagnosis of pleurisy can be made. There are numerous causes of pleurisy, with viral pleurisy among the most common. Other etiologies may be evaluated through additional diagnostic testing in selected patients. Treatment of pleurisy typically consists of pain management with nonsteroidal anti-inflammatory drugs, as well as specific treatments targeted at the underlying cause. (Am Fam Physician 2007;75:1357-64. Copyright © 2007 American Academy of Family Physicians.)

Pleurisy is inflammation of the parietal pleura that typically results in characteristic pleuritic pain and has a variety of possible causes. The term "pleurisy" is often used to refer to a symptom and a condition. It is more precise to use the term "pleurisy" for the condition and "pleuritic pain" to describe the symptom. Pleuritic pain is a key feature of pleurisy; therefore, this article reviews the physiology and classic characteristics of pleuritic pain, focusing on the presentation and diagnosis of the patient and the management of various causes of pleurisy.

Pathophysiology

The visceral pleura does not contain any nociceptors or pain receptors. The parietal pleura is innervated by somatic nerves that sense pain when the parietal pleura is inflamed. Inflammation that occurs at the periphery of the lung parenchyma can extend into the pleural space and involve the parietal pleura, thereby activating the somatic pain receptors and resulting in pleuritic pain. Parietal pleurae of the outer rib cage and lateral aspect of each hemidiaphragm are innervated by intercostal nerves. Pain is localized to the cutaneous distribution of those nerves. The phrenic nerve supplies innervations to the central part of each hemidiaphragm; when these fibers are activated, the sensation of pain is referred to the ipsilateral neck or shoulder.

Differential Diagnosis

It is important that physicians first consider potentially life-threatening disorders such as pulmonary embolism, myocardial infarction, and pneumothorax when a patient presents with pleuritic chest pain.[1-5] One study of a consecutive series of patients presenting to the emergency department with pleuritic chest pain found that 5 percent had a pulmonary embolism[6]; in another study, the proportion was 21 percent.[7] Pericarditis and pneumonia are two other significant causes of pleuritic chest pain that should be considered before pleurisy is diagnosed.[8,9] The differential diagnosis of pleurisy when these causes have been ruled out is presented in *Table 1*.[2,10-18]

Viral infection is one of the most common causes of pleurisy. Viruses that have been linked as causative agents include influenza, parainfluenza, coxsackieviruses, respiratory syncytial virus, mumps, cytomegalovirus, adenovirus, and Epstein-Barr virus.[10-12] Additionally, pleurisy may be the first manifestation of some less-common disorders.

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*
A thorough history and physical examination should be performed to diagnose or exclude life-threatening causes of pleuritic pain before making a diagnosis of pleurisy.	C	3, 9, 19, 22, 29
Pulmonary embolism is the most common life-threatening cause of pleuritic chest pain and should be considered in all patients with this symptom. Evaluation should be performed using validated clinical decision rules, D-dimer testing, and imaging studies as needed.	C	19
Patients with pleuritic pain should have chest radiography to evaluate for underlying pneumonia.	C	9
Nonsteroidal anti-inflammatory drugs should be used to control pleuritic pain.	B	30, 31

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 1289 or http://www.aafp.org/afpsort.xml.

Table 1. Differential Diagnosis of Pleurisy*

Category	*Etiology*
Cardiac	Post–cardiac injury syndrome, post–myocardial infarction syndrome (Dressler's syndrome), postpericardiotomy syndrome (postcommissurotomy syndrome)
Exposure	Asbestosis, some medications†
Gastrointestinal	Inflammatory bowel disease, spontaneous bacterial pleuritis
Genetic	Familial Mediterranean fever
Hematologic/ oncologic	Malignancy, sickle cell disease
Infectious	Viral (e.g., adenovirus, coxsackieviruses, cytomegalovirus, Epstein-Barr virus, influenza, mumps, parainfluenza, respiratory syncytial virus)
	Bacterial (e.g., Mediterranean spotted fever, parapneumonic or tuberculous pleuritis)
	Parasitic (e.g., amebiasis, paragonimiasis)
Inflammatory	Reactive eosinophilic pleuritis
Renal	Chronic renal failure, renal capsular hematoma
Rheumatologic	Lupus pleuritis, rheumatoid pleuritis, Sjögren's syndrome

**—Assumes pulmonary embolism, myocardial infarction, pneumothorax, pericarditis, and pneumonia have been ruled out as the cause of pleuritic chest pain.*
†—Drugs known to cause pleural disease include amiodarone (Cordarone), bleomycin (Blenoxane), bromocriptine (Parlodel), cyclophosphamide (Cytoxan), methotrexate, methysergide (Sansert; not available in the United States), minoxidil (Loniten), mitomycin (Mutamycin), oxyprenolol (Apsolox; not available in the United States), practolol (Eraldin; not available in the United States), procarbazine (Matulane), and sclerotherapeutic agents. Drugs that may cause lupus pleuritis include hydralazine (Apresoline), procainamide (Pronestyl), and quinidine.

Information from references 2 and 10 through 18.

Presentation

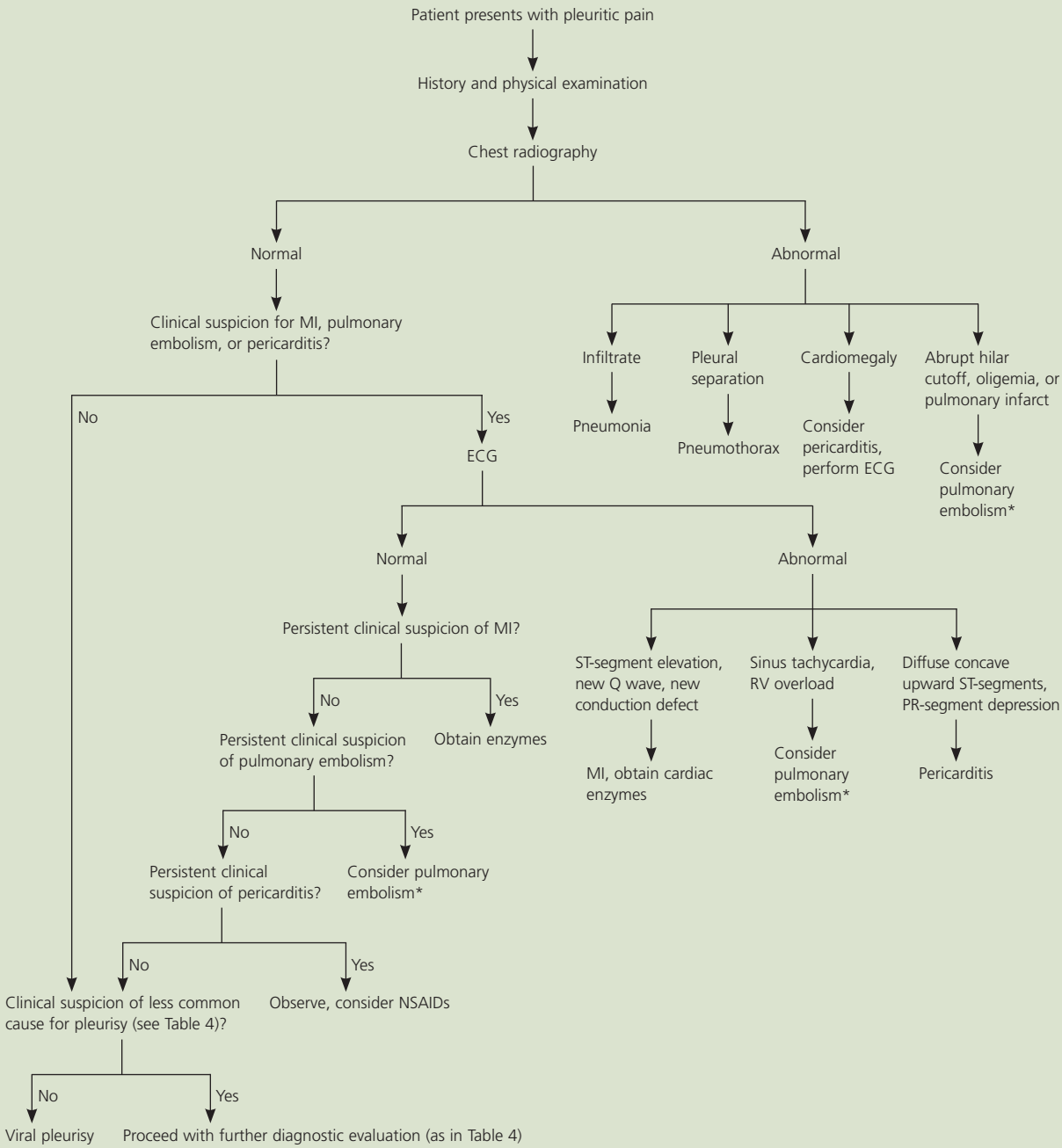
Patients with pleuritic pain present in different ways depending on the underlying cause. Pleuritic pain typically is localized to the area that is inflamed or along predictable referred pain pathways. Patients' descriptions of the pain are consistent in most cases of pleurisy. The classic feature is that forceful breathing movement, such as taking a deep breath, talking, coughing, or sneezing, exacerbates the pain.

Patients often relate that the pain is sharp and is made worse with movement. Typically, they will assume a posture that limits motion of the affected area. Pain with respiration may cause patients to complain of shortness of breath or dyspnea.

Evaluation

A recommended approach for the evaluation of patients presenting with pleuritic chest pain is given in *Figure 1*.[3-5,8,9,19-22] Evaluation of patients in whom pulmonary embolism is suspected should include an assessment of the probability of pulmonary embolism using a validated clinical decision rule, such as the Wells rule,[19] and a D-dimer test. Computed tomography or ventilation-perfusion scanning may be required in patients who are at moderate or high risk or who have an abnormal D-dimer test result.[20]

Outpatient Diagnosis of Pleuritic Pain



NOTE: *This algorithm combines and simplifies diagnostic recommendations from multiple sources to provide an overview and does not represent a validated clinical decision rule.*

**—Apply Wells decision rule to assess pretest probability, order D-dimer and interpret in light of pretest probability, then order further testing as recommended by that diagnostic algorithm.[19,20]*

Figure 1. Algorithm for the outpatient diagnosis of pleuritic pain. (MI = myocardial infarction; ECG = electrocardiography; RV = right ventricular; NSAIDs = nonsteroidal anti-inflammatory drugs.)

Information from references 3 through 5, 8, 9, and 19 through 22.

Table 2. Etiologies of Pleuritic Pain by Symptom Onset

Onset	*Etiologies*
Acute (i.e., minutes to hours)	Myocardial infarction Pulmonary embolism Spontaneous pneumothorax Trauma
Subacute (i.e., hours to days)	Infection Inflammatory process
Chronic (i.e., days to weeks)	Malignancy Rheumatoid arthritis Tuberculosis
Recurrent	Familial Mediterranean fever

Information from reference 2.

MEDICAL HISTORY

A careful, focused history is the first step in identifying the underlying etiology of pleuritic pain. A key question is the time course of the onset of symptoms *(Table 2[2])*.

Although pleuritic pain decreases the likelihood that a patient with chest pain is experiencing myocardial ischemia, it does not eliminate the possibility.[3] If other history findings suggest this diagnosis, further evaluation with electrocardiography (ECG) and cardiac enzymes, as well as close observation, is indicated. Pain that worsens while the patient is supine and lessens while the patient is upright should prompt consideration of pericarditis.[8,21] Dyspnea associated with the pain should raise clinical suspicion for pulmonary embolism, pneumonia, and pneumothorax.[5,9,23]

Features that are associated with life-threatening causes of pleuritic pain are listed in *Table 3*.[3-5,8,9,21,22] Other symptoms, such as malaise, weight loss, night sweats, and joint pains, may indicate one of the less-common causes of pleurisy. It is important to investigate the patient's underlying medical conditions, medication list, and recent travel history, and to take a history of similar symptoms in family members. A selected differential diagnosis with associated clinical results is listed in *Table 4*.[13-18,24-27]

Table 3. Findings Associated with Life-Threatening Causes of Pleuritic Pain

Diagnosis	*History*	*Physical examination*	*Chest radiography*	*Electrocardiography*
Myocardial infarction	Substernal pain that radiates, dyspnea, shortness of breath Pleuritic pain decreases likelihood ratio	Diaphoresis, hypotension, third heart sound (S_3)	Usually normal	ST-T elevations (especially if new), new Q wave, new conduction defect
Pericarditis	Positional pain: increases while supine and decreases when upright	Pericardial friction rub	Increased heart size with pericardial effusion greater than 250 mL	Diffuse concave upward ST-segments, PR-segment depression Abnormality noted in more than 90 percent of cases
Pneumonia	Anorexia, cough, dyspnea, fatigue, myalgia	Crackles, egophony, fremitus	Infiltrate	Typically not indicated
Pneumothorax	Sudden pain and dyspnea	Tachycardia, hyperresonance, decreased breath sounds, decreased wall movement	Thin pleural line May be normal in small pneumothorax	Typically not indicated Sinus tachycardia
Pulmonary embolism	Prior embolism or clot Cancer, immobilization, estrogen use, or recent surgery Dyspnea, syncope	Tachycardia, tachypnea	Abrupt hilar cutoff, oligemia, or pulmonary consolidations compatible with infarction	Sinus tachycardia, right ventricular overload (T-wave inversion in right precordial leads, S_1Q_3/$S_1Q_3T_3$, transient right bundle branch block, pseudoinfarction, $S_1S_2S_3$)

Information from references 3 through 5, 8, 9, 21, and 22.

Table 4. Findings Associated with Selected Causes of Pleurisy

Diagnosis	*History*	*Physical examination*	*Selected diagnostic test results*
Connective tissue disorders	Prior diagnosis of systemic lupus erythematosus, rheumatoid arthritis, or other connective tissue disorder should raise suspicion, but pleuritic chest pain may be initial presentation Fever; arthritis or arthralgias	Decreased breath sounds	Chest radiography: small to moderate unilateral or bilateral effusion PFA: exudative effusion (rheumatoid arthritis characterized by low glucose level [< 40 mg per dL (2.2 mmol per L)], elevated lactic dehydrogenase level [> 700 U per L], and low pH [< 7.2]) Abnormal disease-specific serologic markers
Drug-induced pleuritis	Use of drug known to cause drug-induced pleural disease or drug-induced lupus pleuritis*	Possible decreased breath sounds, pleural friction rub	Chest radiography: may be normal or demonstrate infiltrate, pleural effusion, or pleural thickening PFA: exudative effusion
Familial Mediterranean fever	Recurrent episodes of fever (one to four days) associated with abdominal, chest, or joint pain or erysipelas-like skin disease Mediterranean descent Family history of familial Mediterranean fever	Normal between episodes During episodes: temperature of 100 to 104°F (38 to 40°C) and signs of serositis (e.g., peritoneal irritation, pleural and/or pericardial friction rub) Other possible findings: joint swelling, unilateral erythema over extensor surface of leg, ankle, or foot	Increased acute phase reactants (ESR, CRP, WBC, fibrinogen) Positive mutation analysis for *MEFV* gene
Post–cardiac injury syndrome†	Recent myocardial infarction, cardiac procedure, or chest trauma Fever, dyspnea, pleuropericardial pain	Pleural and/or pericardial friction rub; decreased breath sounds	Chest radiography: may reveal pleural effusion PFA: exudative effusion Elevated ESR, leukocytosis Electrocardiographic abnormalities similar to pericarditis (see Table 3)
Tuberculous pleuritis	Exposure to environment with high risk of *Mycobacterium tuberculosis* Cough, low-grade fever, weight loss, fatigue Human immunodeficiency virus infection	Unilaterally decreased breath sounds	Chest radiography: small to moderate unilateral pleural effusion, often without associated infiltrate PFA: exudative effusion with elevated adenosine deaminase levels (> 40 to 60 U per L [670 to 1,000 nkat per L]) Caseous granulomas on pleural biopsy Culture positive for *M. tuberculosis* on induced sputum, pleural fluid culture, or pleural biopsy Negative PPD result does not exclude diagnosis
Viral pleurisy	Recent respiratory illness or undifferentiated febrile illness	Rapid, shallow respirations; pleural friction rub	Chest radiography: normal

PFA = pleural fluid analysis; ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; WBC = white blood cell count; PPD = purified protein derivative.

**—Drugs known to cause pleural disease include amiodarone (Cordarone), bleomycin (Blenoxane), bromocriptine (Parlodel), cyclophosphamide (Cytoxan), methotrexate, methysergide (Sansert; not available in the United States), minoxidil (Loniten), mitomycin (Mutamycin), oxyprenolol (Apsolox; not available in the United States), practolol (Eraldin; not available in the United States), procarbazine (Matulane), and sclerotherapeutic agents. Drugs that may cause lupus pleuritis include hydralazine (Apresoline), procainamide (Pronestyl), and quinidine.*

†—Post–cardiac injury syndrome includes post–myocardial infarction syndrome (Dressler's syndrome) and postpericardiotomy syndrome (postcommissurotomy syndrome).

Information from references 13 through 18 and 24 through 27.

PHYSICAL EXAMINATION

The normally smooth surfaces of the parietal and visceral pleurae become rough with inflammation. As these surfaces rub against one another, a rough scratching sound, or friction rub, may be heard with inspiration and expiration. This friction rub is a classic feature of pleurisy. It may also occur in about 4 percent of patients with pneumonia and 4 percent of patients with pulmonary embolism.[28] Additional physical findings on the pulmonary examination may include decreased breath sounds, rales, and egophony, especially in patients with underlying pneumonia.[9]

Other physical examination findings that raise clinical suspicion for certain conditions include the pericardial rub of pericarditis[5] and the hyperresonance and decreased wall movement that occur with pneumothorax.[8] Physical examination findings associated with life-threatening conditions that cause pleuritic pain are listed in *Table 3*.[3-5,8,9,21,22] Further physical examination is directed by the etiology suggested by the clinical history. It is important to remember that patients with any of these serious conditions who present with pleuritic pain may have a normal physical examination, and a high index of suspicion and further diagnostic testing are often indicated.

Table 5. Initial Evaluation of Pleural Fluid

Quality	*Test indicated*	*Interpretation*
Appearance		
Bloody	Hematocrit	< 1 percent: nonsignificant 1 to 20 percent: cancer, pulmonary embolus, or trauma > 50 percent peripheral hematocrit: hemothorax
Cloudy or turbid	Centrifugation	Turbid supernatant: chylothorax
Odor		
Putrid	Stain and culture	Possible anaerobic infection
Distinguishing transudate from exudate		
Light's criteria	Fluid is exudate if it meets one or more of the following criteria:	Ratio of pleural fluid protein level to serum protein level > 0.5 Ratio of pleural fluid LDH level to serum LDH level > 0.6 Pleural fluid LDH level > two thirds the upper limit of normal for serum LDH level
Confirmation of Light's criteria assessment*	Fluid is exudate if:	Serum albumin level – pleural fluid albumin level ≤ 1.2 g per dL (12 g per L)

LDH = lactate dehydrogenase.

**—To use when patient's clinical appearance suggests transudative effusion.*

Adapted with permission from Light RW. Pleural effusion. N Engl J Med 2002; 346:1974.

DIAGNOSTIC TESTS

Because pleuritic chest pain may be a presenting complaint for pneumonia, pulmonary embolism, or pneumothorax,[1,9] all patients presenting with this symptom should have chest radiography. Additionally, pleurisy often is associated with a pleural effusion, which can be identified on a chest radiograph. Pleural fluid can be examined for further etiologic clues *(Table 5*[29]*)*.

ECG evaluation is recommended if there is clinical suspicion of myocardial infarction, pulmonary embolism, or pericarditis.[3,21,28] Typical ECG findings associated with these conditions are listed in *Table 3*.[3-5,8,9,21,22] When the etiology of pleurisy is other than viral, further diagnostic testing may be indicated in selected patients *(Table 4*[13-18,24-27]*)*.

Treatment

Management of pleurisy has two primary goals: (1) control the pleuritic chest pain, and (2) treat the underlying condition. To achieve pain control, nonsteroidal anti-inflammatory drugs (NSAIDs) commonly are prescribed as the initial therapy. Narcotic analgesics may be required to relieve severe pleuritic chest pain; however, NSAIDs do not suppress respiratory efforts or cough reflex and are the preferred first-line agent.

Although a class effect is presumed, human studies on the use of NSAIDs to treat pleuritic chest pain have been limited to indomethacin (Indocin). Indomethacin, in dosages of 50 to 100 mg orally up to three times per day with food, has been found to be effective in relieving pleural pain, with associated improvement in mechanical lung

function.[30,31] Supportive care with adequate pain control is the goal in the treatment of viral pleurisy.

To achieve the second management goal, therapies are selected based on the underlying condition. If a patient has suspected drug-induced pleuritis or drug-induced lupus pleuritis, the causal agent should be discontinued.[16,17] Smoking cessation should be advised for patients with pleurisy caused by asbestosis.[32] Antimicrobial and antiparasitic agents are selected empirically based on the suspected underlying organism. Decortication is considered in cases of pleuritis associated with refractory pleural effusions resulting from malignancy, chronic renal failure, or rheumatoid pleurisy.[2] Colchicine (1.2 to 2.0 mg orally once per day, or twice per day in a divided dose) is the mainstay of treatment for familial Mediterranean fever.[18]

NSAIDs are first-line therapy for patients with post–cardiac injury syndrome; corticosteroids are reserved for those who are intolerant of or experience no response to NSAIDs.[14] Although oral corticosteroids are recommended for patients with lupus pleuritis, they have not been demonstrated to influence the course of rheumatoid pleuritis.[2,15]

The role of systemic corticosteroids in the treatment of tuberculous pleuritis is controversial. Tuberculous pleuritis is associated with inflammation and fibrosis, and a small number of randomized and quasi-randomized studies with patients who did not have human immunodeficiency virus have assessed the impact of steroids on this process.[33] No difference was detected in the primary outcome of an alteration in residual lung function. Although these studies did show a trend toward benefit (reduction in the number of patients with pleural effusions, thickening, or adhesions), there is insufficient evidence to determine whether steroids are an effective treatment.[33]

The opinions and assertions contained herein are the private views of the authors and are not to be construed as official or as reflecting the views of the Uniformed Services University, the U.S. Navy, the U.S. Air Force, or the Department of Defense.

The Authors

SARA M. KASS, CDR, MC, USN, is an assistant professor in the Department of Family Medicine at the Uniformed Services University of the Health Sciences in Bethesda, Md. Dr. Kass graduated from the George Washington University School of Medicine and Health Sciences in Washington, D.C. She completed a residency in family medicine at Puget Sound Family Medicine Residency, Bremerton, Wash.

PAMELA M. WILLIAMS, MAJ, USAF, MC, is an assistant professor in the Department of Family Medicine at the Uniformed Services University of the Health Sciences. Dr. Williams graduated from the University of Pennsylvania School of Medicine in Philadelphia. She completed a residency in family practice at David Grant USAF Medical Center, Travis Air Force Base, Calif., and a fellowship in faculty development with the University of California, San Francisco, School of Medicine.

BRIAN V. REAMY, COL, USAF, MC, is chair of the Department of Family Medicine at the Uniformed Services University of the Health Sciences. Dr. Reamy graduated from Georgetown University Medical Center School of Medicine in Washington, D.C. He completed a residency in family practice at David Grant USAF Medical Center and a fellowship in faculty development at the University of California, San Francisco, School of Medicine.

Address correspondence to Sara M. Kass, CDR, MC, USN, Uniformed Services University of the Health Sciences, 4301 Jones Bridge Rd., Bethesda, MD 20814 (e-mail: smkass@us.med.navy.mil). Reprints are not available from the authors.

Author disclosure: Nothing to disclose.

REFERENCES

1. Staton GW Jr, Ingram RH Jr. IX. Disorders of the pleura, hila, and mediastinum. In: Holtzman MJ. ACP Medicine: 14. Respiratory medicine. Danbury, Conn.: WebMD, 2005. Accessed December 19, 2006, at: http://www.acpmedicine.com/abstracts/sam/med1409.htm.
2. Nadel JA, Murray JF, Mason RJ. Textbook of Respiratory Medicine. 4th ed. Philadelphia, Pa.: Saunders, 2005:254, 497-8, 856, 1946, 1993, 2235.
3. Panju AA, Hemmelgarn BR, Guyatt GH, Simel DL. The rational clinical examination. Is this patient having a myocardial infarction? JAMA 1998;280:1256-63.
4. Poulsen SH, Noer I, Moller JE, Knudsen TE, Frandsen JL. Clinical outcome of patients with suspected pulmonary embolism. A follow-up study of 588 consecutive patients. J Intern Med 2001;250:137-43.
5. Sahn SA, Heffner JE. Spontaneous pneumothorax. N Engl J Med 2000;342:868-74.
6. Hogg K, Dawson D, Mackway-Jones K. The emergency department utility of Simplify D-dimer to exclude pulmonary embolism in patients with pleuritic chest pain. Ann Emerg Med 2005;46:305-10.
7. Hull RD, Raskob GE, Carter CJ, Coates G, Gill GJ, Sackett DL, et al. Pulmonary embolism in outpatients with pleuritic chest pain. Arch Intern Med 1988;148:838-44.
8. Goyle KK, Walling AD. Diagnosing pericarditis. Am Fam Physician 2002;66:1695-702.

9. Metlay JP, Kapoor WN, Fine MJ. Does this patient have community-acquired pneumonia? Diagnosing pneumonia by history and physical examination. JAMA 1997;278:1440-5.
10. Bungetianu G, Galbenu P, Petrescu A, Athanasiu P, Verner A, Ghinescu C, et al. Contributions to the study of the etiology of serofibrinous pleurisy in Romania, under the present epidemiological conditions. Evaluation of the etiological role of viruses. Virologie 1984;35:11-9.
11. Harley RA. Pathology of pleural infections. Semin Respir Infect 1988;3:291-7.
12. Frasca A, Smeraglia R, Tarro G, Caserta I, Scala C, Salerno M, et al. Association between viral infection and pleuropericarditis: study of a case list of pleurisy and pericarditis [Italian]. Boll Ist Sieroter Milan 1980;59:112-20.
13. Qiu L, Teeter LD, Liu Z, Ma X, Musser JM, Graviss EA. Diagnostic associations between pleural and pulmonary tuberculosis. J Infect 2006;53:377-86.
14. Wessman DE, Stafford CM. The postcardiac injury syndrome: case report and review of the literature. South Med J 2006;99:309-14.
15. Aiello M, Chetta A, Marangio E, Zompatori M, Olivieri D. Pleural involvement in systemic disorders. Curr Drug Targets Inflamm Allergy 2004;3:441-7.
16. Huggins JT, Sahn SA. Drug-induced pleural disease. Clin Chest Med 2004;25:141-53.
17. Rubin RL. Drug-induced lupus. Toxicology 2005; 209:135-47.
18. Ben-Chetrit E, Levy M. Familial Mediterranean fever. Lancet 1998;351:659-64.
19. Wells PS, Anderson DR, Rodger M, Stiell I, Dreyer JF, Barnes D, et al. Excluding pulmonary embolism at the bedside without diagnostic imaging: management of patients with suspected pulmonary embolism presenting to the emergency department by using a simple clinical model and D-dimer. Ann Intern Med 2001;135:98-107.
20. Ebell MH. Suspected pulmonary embolism: evidence-based diagnostic testing. Am Fam Physician 2004;69:599-601.
21. Marinella MA. Electrocardiographic manifestations and differential diagnosis of acute pericarditis. Am Fam Physician 1998;57:699-704.
22. Stein PD, Terrin ML, Hales CA, Palevsky HI, Saltzman HA, Thompson BT, et al. Clinical, laboratory, roentgenographic, and electrocardiographic findings in patients with acute pulmonary embolism and no pre-existing cardiac or pulmonary disease. Chest 1991;100:598-603.
23. Perrier A, Roy PM, Aujesky D, Chagnon I, Howarth N, Gourdier AL, et al. Diagnosing pulmonary embolism in outpatients with clinical assessment, D-dimer measurement, venous ultrasound, and helical computed tomography: a multicenter management study. Am J Med 2004;116:291-9.
24. Kataria YP, Khurshid I. Adenosine deaminase in the diagnosis of tuberculous pleural effusion. Chest 2001;120:334-6.
25. Greco S, Girardi E, Masciangelo R, Capoccetta GB, Saltini C. Adenosine deaminase and interferon gamma measurements for the diagnosis of tuberculous pleurisy: a meta-analysis. Int J Tuberc Lung Dis 2003;7:777-86.
26. Conde MB, Loivos AC, Rezende VM, Soares SL, Mello FC, Reingold AL, et al. Yield of sputum induction in the diagnosis of pleural tuberculosis. Am J Respir Crit Care Med 2003;167:723-5.
27. Akar N, Akar E, Ozel D, Tekin M, Ekim M, Yalcinkaya F. A note on the mutation analysis in familial Mediterranean fever. Pediatr Nephrol 2003;18:196-7.
28. Miniati M, Prediletto R, Formichi B, Marini C, Di Ricco G, Tonelli L, et al. Accuracy of clinical assessment in the diagnosis of pulmonary embolism. Am J Respir Crit Care Med 1999;159:864-71.
29. Light RW. Pleural effusion. N Engl J Med 2002;346: 1971-7.
30. Sacks PV, Kanarek D. Treatment of acute pleuritic pain. Comparison between indomethacin and a placebo. Am Rev Respir Dis 1973;108:666-9.
31. Klein RC. Effects of indomethacin on pleural pain. South Med J 1984;77:1253-4.
32. Nelson HH, Kelsey KT. The molecular epidemiology of asbestos and tobacco in lung cancer. Oncogene 2002;21:7284-8.
33. Matchaba PT, Volmink J. Steroids for treating tuberculous pleurisy. Cochrane Database Syst Rev 2000;(1): CD001876.