

## Recurrent Symptomatic Pleural Effusions: Approaches to Diagnosis of a Difficult Problem

Pleural effusions, seen in isolation or in association with a number of pulmonary and systemic diseases, are common problems in both the in-patient and out-patient setting. The incidence of pleural effusion in the general population is hard to estimate. Reports suggest an incidence of 0.3% in the general population, with as many as 800,000 cases annually. Pleural effusions frequently complicate malignant disease, heart and liver diseases, infections, and other rare diseases.<sup>1</sup>

The diagnostic approach to pleural effusion is multifaceted, beginning with a careful clinical assessment and followed by radiologic, laboratory, and cytopathology studies. History provides useful information, such as exposure to asbestos, suggesting mesothelioma or drug-induced pleural disease. Proper studies aid in the diagnosis, recognition of the problem, and disease state. Typical symptoms include dyspnea, cough, and chest pain. Physical signs include asymmetric chest expansion, dullness to percussion, decreased to absent breath sounds, reduced vocal fremitus, and pleura rub. In a cohort of symptomatic patients with respiratory conditions, asymmetric chest expansion and dullness to percussion had adjusted odds ratios of 5.3 and 12.8, respectively, for pleural effusions.<sup>2</sup> Except in cases of large pleural effusions, initial imaging confirms and evaluates the size and characteristic of the pleural space. The amount of pleural fluid can be estimated from radiography. Studies have suggested that as little as 75 mL can be detected in the posterior costophrenic sulcus, whereas, a minimum of 175 mL is necessary to obscure the lateral sulcus.<sup>3-5</sup> Ultrasound is superior in clarifying the nature of a pleural fluid and the detection of smaller effusions, compared to conventional radiography and physical examination. Studies have found effusions as small as 5–50 mL with careful ultrasound.<sup>6</sup> Computed tomography is unequaled in its ability to depict the entire pleural space, simultaneously imaging the pulmonary parenchyma and mediastinum.

There are 2 categories of pleural effusions: transudative and exudative. In most circumstances the gross appearance of the pleural fluid can help identify effusion type. Purulent fluid indicates an infection. Milky white fluid could represent a chylous effusion. Bloody fluid or hemothorax results from trauma or instrumentation but may be observed in malignancy. Pleural effusions are always sec-

ondary to a disease process. Some effusions can simply be observed; new, unilateral, and enlarging effusions or failure of an effusion to resolve with treatment indicates the need for diagnostic thoracenteses. The investigative work involved in the diagnosis can be mapped out in an algorithm and includes testing.<sup>7</sup> The first step consists in establishing type. If the fluid is transudative, the differential diagnosis is narrowed. Typically, exudative effusions require additional testing.

Since its original publication, Light's criteria have been widely used to separate exudates and transudates.<sup>8</sup> Perhaps the only limitation of these criteria is the need for concomitant blood draw for measurement of serum lactate dehydrogenase and protein. Other alternative markers have been proposed, although serial different reports have failed to show a significant advantage with other markers.<sup>9</sup> Using Light's criteria, the physician can be confident in correcting almost all exudative effusions. However, a specific problem using Light's criteria occurs in patients with congestive heart failure treated with diuretics. Another option, particularly helpful when serum levels of lactate dehydrogenase and protein are not available, is to measure cholesterol levels. Meta-analysis suggested that a cholesterol level > 45 mg/dL identifies exudates with an accuracy similar to Light's criteria.<sup>10</sup>

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In this issue of *RESPIRATORY CARE*, Irani and colleagues report on a recurrent symptomatic exudative pleural effusion,<sup>11</sup> and they outline the difficulties in diagnosing a recurrent effusion. Importantly, they allow the history, physical, and details of the pleural effusion to help narrow the differential diagnosis. One interesting aspect of this case report is the use of specific laboratory tests to confirm a diagnosis. Although almost any serum tests can be ordered on pleural fluid, many do not have "normal" reference ranges. The lack of reference levels makes their utility difficult when it comes to diseases affecting the pleural cavity. Irani and colleagues used  $\beta_2$  transferrin to help confirm a diagnosis of a ventriculopleural shunt.  $\beta_2$  transferrin has been widely used to identify cerebrospinal fluid leakage following head trauma, as it is found only in cerebrospinal fluid and inner-ear perilymph fluid. Subarach-

noid pleural fistulas are usually a complication of penetrating and blunt trauma, thoracic surgery, and spinal surgery, and remain rare. The majority of the cases reported to date have been due to blunt and penetrating trauma (23 of 30 cases, 77%).<sup>12</sup> In fact, the etiology of the effusion reported by Irani and colleagues makes this report rare and important. Regardless of the cause, a high degree of suspicion is required to establish the diagnosis of a central nervous system pleural fistula. The use of electrophoresis for  $\beta_2$  transferrin aids in identifying cerebrospinal fluid in the pleural fluid. The test is both sensitive (100%) and specific (95%) for cerebrospinal fluid leaks.<sup>13,14</sup> In general, the workup for pleural effusions requires diligence. Making a correct diagnosis can be difficult, and understanding the various diagnostic techniques and their limitations is important in identifying the causes of the underlying disease process.

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## REFERENCES

1. Marel M, Zrůstová M, Stasný B, Light RW. The incidence of pleural effusion in a well-defined region: epidemiologic study in central Bohemia. *Chest* 1993;104(5):1486-1489.
2. Kalantri S, Joshi R, Lokhande T, Singh A, Morgan M, Colford JM Jr, Pai M. Accuracy and reliability of physical signs in the diagnosis of pleural effusion. *Respir Med* 2007;101(3):431-438.
3. Evans AL, Gleeson FV. Radiology in pleural disease: state of the art. *Respirology* 2004;9(3):300-312.
4. Woodring JH. Recognition of pleural effusion on supine radiographs: how much fluid is required? *AJR Am J Roentgenol* 1984;142(1):59-64.
5. Woodring JH. Detection of pleural effusion on supine chest radiographs. *AJR* 1987;149(4):858-859.
6. Qureshi NR, Gleeson FV. Imaging of pleural disease. *Clin Chest Med* 2006;27(2):193-213.
7. Diaz-Guzman E, Dweik RA. Diagnosis and management of pleural effusions: a practical approach. *Compr Ther* 2007;33(4):237-246.
8. Light RW, Macgregor MI, Luchsinger PC, Ball WC Jr. Pleural effusions: the diagnostic separation of transudates and exudates. *Ann Intern Med* 1972;77(4):507-513.
9. Romero S, Candela A, Martín C, Hernández L, Trigo C, Gil J. Evaluation of different criteria for the separation of pleural transudates from exudates. *Chest* 1993;104(2):399-404.
10. Heffner JE, Sahn SA, Brown LK. Multilevel likelihood ratios for identifying exudative pleural effusions. *Chest* 2002;121(6):1916-1920.
11. Irani F, Elkambergy H, Okoli K, Abou Abdallah DS. Recurrent symptomatic pleural effusion due to a ventriculopleural shunt. *Respir Care* 2009;54(8):1112-1114.
12. Lloyd C, Sahn SA. Subarachnoid pleural fistula due to penetrating trauma: case report and review of the literature. *Chest* 2002;122(6):2252-2256.
13. Skedros DG, Cass SP, Hirsch BE, Kelly RH. Beta-2 transferrin assay in clinical management of cerebral spinal fluid and perilymphatic fluid leaks. *J Otolaryngol* 1993;22(5):341-344.
14. Skedros DG, Cass SP, Hirsch BE, Kelly RH. Sources of error in use of beta-2 transferrin analysis for diagnosing perilymphatic and cerebral spinal fluid leaks. *Otolaryngol Head Neck Surg* 1993;109(5):861-864.