

# EPEEC-O

Education in Palliative and End-of-life Care - Oncology

## **Participant's Handbook**

Module 3m:

**Symptoms –**

**Malignant**

**Pleural**

**Effusions**

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## Case\*

F.G., an 84-year-old former truck driver with stage IV lung cancer, reported gradually progressive dyspnea over 2 weeks. He was diagnosed with T4N2M1 adenocarcinoma of the right lung with 3 liver metastases 6 months prior to this visit. He received 4 cycles of cisplatin, docetaxel with partial response. Treatment was stopped when his performance status deteriorated from 1 to 3. Since chemotherapy was stopped, his performance status improved to 2 until the past 2 weeks when it again deteriorated to 3. Evaluation revealed progressive disease in the liver and a new large left pleural effusion estimated at 3 liters on the chest radiograph. Thoracentesis revealed an exudate and produced partial relief of dyspnea. A radiographically placed catheter was placed and his wife was taught how to manage the drainage. Sclerosis was considered, but not performed due to high flow rates (>500 ml/day) and poor performance status. Hospice care was begun. He died comfortably at home 4 weeks later.

\* This case is not on an EPEC-O Curriculum trigger tape.

## Introduction

Pleural effusions accumulate in the potential space between the visceral (inner) layer covering the lungs and the parietal (outer) layer covering the chest wall. The most commonly associated symptom is dyspnea, although persistent cough and chest pain can also occur.

## Prevalence

Malignant pleural effusions occur commonly in patients with cancer. The malignancies responsible for more than 75% of all of pleural effusions in order of frequency are lung, breast, lymphoma, and ovarian cancer.

In a general hospital setting, 25% of all pleural effusions are malignant. In patients with an existing diagnosis of cancer, this increases to 30-70% if the fluid is an exudate.

## Prognosis

A pleural effusion from a malignancy for which there is no effective treatment portends a poor prognosis. Median survival for patients with an effusion due to metastatic cancer averages 3 months. Drainage alone does not affect survival, only comfort.<sup>1</sup>

## Pathophysiology

Normally, there is less than 20 ml of fluid in the pleural space, this provides lubrication during breathing. This volume is normally in equilibrium between secretion by the parietal pleura and absorption by the visceral pleura in the lymphatic system. Up to 10 liters of low protein fluid flows through the space each day.

Fluid accumulates when this balance is disrupted by decreased oncotic pressure, eg, decreased serum albumin, or increased lymphatic system pressure, eg, infiltration by

tumor. In addition, metastases to the pleural space can disrupt flow through direct disruption of the pleural surfaces and associated inflammation.

## Assessment

A history of worsening dyspnea, cough, and/or pleuritic chest pain may suggest a pleural effusion.

Diminished breath sounds, fremitus, and dullness to percussion on physical examination are suggestive.

Chest radiographs establish the probability of the effusion and provide an estimate of volume. Lateral decubitus views can distinguish free-flowing from loculated effusions. Computed tomography scans are useful when radiographs are inconclusive.

The diagnosis is made with thoracentesis. A clinically significant pleural effusion of unknown cause is an indication for thoracentesis.<sup>2</sup> Collect a small volume of fluid to evaluate its composition, cytology and complete cell count. Perform culture and sensitivities if infection is suspected. Twenty five percent of all pleural effusions in a general hospital are malignant.<sup>2</sup> In patients with an existing diagnosis of cancer, this increases to 30-70% if the fluid shows an exudate.<sup>1</sup>

Measure both pleural fluid and serum total protein, glucose, lactose dehydrogenase, and pH. Effusions are evaluated as transudative or exudative based on Light's criteria.<sup>1</sup> Transudative effusions are rarely malignant. If the clinical appearance of the fluid suggests a transudate but according to Light's criteria is an exudate, measure the difference between the serum and pleural fluid albumin. Generally, a serum albumin level > 1.2 g/dl above the pleural fluid albumin level is consistent with a transudative effusion.<sup>3</sup> A meta-analysis of studies that discriminate between exudative and transudative effusions determined alternate thresholds for LDH (pleural LDH > 0.45 ULN), pleural cholesterol (>45mg/dl) and pleural protein (>2.9 g/d).<sup>4</sup>

**Table 1: Light's criteria for transudative vs. exudative effusions**

	Transudate	Exudate
<b>Malignant Cells</b>	Negative	Positive < 50%
<b>Cell count</b>	Low	high
<b>Total protein</b>	Pleural : serum ratio < 0.5	Pleural : serum ratio > 0.5
<b>LDH</b>	Pleural : serum ratio < 0.6	Pleural : serum ratio > 0.6 or > 2/3 normal serum limit
<b>pH</b>	< 7.3	> 7.3

In 25% of patients with cancer and recurrent pleural effusion, malignant cells may not be identified by cytology.<sup>5</sup> Three pleural fluid samples increase the yield to 77%. In such cases, thoracoscopy with pleural biopsy is more likely to be diagnostic.<sup>2</sup>

## Management

### Drainage

Establish the goals of treatment before initiating drainage. Consider the patient's symptoms, performance status, primary site of the tumor and its responsiveness to available antineoplastic treatment, and potential for lung expansion following drainage of fluid. Drainage may achieve goals of relief of dyspnea, minimize hospitalization, improve function, and give the patient and family a sense of control.

A new diagnosis of non-small cell lung cancer, breast cancer, lymphoma, or germ cell cancer may best be managed with chemotherapy if the patient has an adequate performance status.

A variety of options, as listed below along with the advantages and disadvantages of each, are available for drainage.

**Table 2: Thorax drainage options**

	<b>Advantages</b>	<b>Disadvantages</b>
<b>Serial thoracentesis</b>	Technically simple. Can be performed at home or in outpatient setting. Volumes large enough to cause symptoms make pneumothorax unlikely. Avoid removal of >1500cc.	Impractical with quickly reaccumulating fluid. Recurrence rate at one month approaches 100%. <sup>6</sup>
<b>Chest tube insertion with intrapleural sclerosant</b>	Success rate > 60%, low incidence of complications. Small bore (10-14F) equally as effective as large bore tubes. <sup>7</sup>	Side effects of sclerosants and pain. Requires hospitalization.
<b>Permanent or semipermanent catheter</b>	Placed by interventional radiology or surgery. Can be continuous or intermittent drainage. Family can manage catheter.	Highly proteinaceous fluid may clog. Local cellulitis most common complication.
<b>Thoracoscopy with talc</b>	High success rate >90%. Perioperative mortality<0.5%.	Surgery required/invasive procedure. Most common major complications: empyema, respiratory failure.
<b>Pleuroperitoneal (Denver) shunt</b>	No external catheters. May be effective for patient with failed pleurodesis.	Patient or caregiver must press pump to be effective. Occlusion, infection risk tumor seeding.

## Thoracoscopy

Thoracoscopy is now the most widely used technique for the management of pleural effusions. It should be considered for the diagnosis of suspected, but unproven, malignant pleural effusion, and for control of recurrent malignant effusions.<sup>6</sup>

Video-assisted thoracoscopy offers multiple advantages over other surgical methods. It offers detailed visualization of the hemithorax, allowing for directed pleural biopsies, therapeutic pleurectomies, mechanical pleurodesis, chemical pleurodesis improved distribution of the sclerosing agent, and catheter placement for thoracic drainage.<sup>6,8</sup>

Patients undergoing video-assisted thoracoscopy have reduced operative time, drainage time, and post operative mobility compared to the open surgical technique.<sup>8</sup> They also experience less pain and less pulmonary dysfunction during the post treatment period than those undergoing mini-thoracotomy.<sup>8</sup>

Patients with 'trapped lung' from a 'rind' of tumor or fibrosis, or an obstructed bronchus will not experience relief of dyspnea, chest pain or cough after thoracentesis. Vigorous manipulation of a chest tube is more likely to cause discomfort, intrapleural infection and emphysema as it is to re-expand the collapsed lung. In carefully selected patients, video-assisted thoracoscopy may offer a therapeutic benefit.<sup>6,8</sup>

## Pleurodesis

Selected patients who have undergone thoracentesis may be candidates for pleurodesis. Typically, patients are candidates if thoracentesis resulted in lung re-expansion with apposition of the visceral and parietal pleura and relief of the symptoms and have < 200 ml/day of drainage.

Pleurodesis is performed to scar the visceral and parietal pleura together and obliterate the potential pleural space. Pleurodesis requires a diffuse inflammatory response and local activation of the coagulation system with fibrin deposition. Talc is generally considered the preferred agent.<sup>9</sup> Pleurodesis can be achieved via chest tube or with a long term indwelling pleural catheter. To date, the only randomized trial compares symptomatic, recurrent malignant pleural effusions. Doxycycline pleurodesis was compared with an indwelling long term intercostals catheter. The degree of improvement in dyspnea was equal and the hospitalization time was shorter for patients with the long term catheter.<sup>10</sup>

Sclerosing agents can produce pain. Therefore, adequate medication with opioids before and after the procedure is required. In addition, sclerosing agents can produce fever, tachycardia, and nausea. Talc, doxycycline, and bleomycin have all been reported to be effective in  $\geq 50\%$  of cases.

Pleuroperitoneal shunts may be useful for patients with a trapped lung or failed pleurodesis.

## Summary

A malignant pleural effusion is associated with an average prognosis of 3 months. In addition to managing dyspnea and pain with opioids, physical drainage of the fluid may relieve symptoms quickly. For fluid that reaccumulates, pleurodesis may prevent the effusion from recurring. A semi-permanent catheter may be placed for frequent drainage in cases where pleurodesis is not possible.

## Key take-home points

1. History, physical examination, and plain radiograph of the chest usually make the diagnosis.
2. Drainage with video-assisted thoracoscopy can provide diagnosis and definitive management.
3. Serial thoracentesis or semi-permanent catheters may be used for effusions for which pleurodesis is not possible, or has failed.

## Pearls

1. Drainage of a large pleural effusion may safely be tapped at home; ultrasound guidance is not required.

## Pitfalls

1. When a patient has a short time to live, use medical management alone.
2. An asymptomatic pleural effusion cannot have its symptoms improved.

## References

- <sup>1</sup> Putnam JB. Malignant pleural effusions. *Surg Clin N Am*. 2002;38:375-383.  
This is a review of the epidemiology, assessment, and treatment of malignant pleural effusions.
- <sup>2</sup> Light RW. Clinical practice. Pleural effusion. *N Engl J Med*. 2002 Jun 20;346(25):1971-1977. [PMID: 12075059](#). [Full Text](#)  
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- <sup>3</sup> Burgess LJ, Maritz FJ, Taljaard JJ. Comparative analysis of the biochemical parameters used to distinguish between pleural transudates and exudates. *Chest*. 1995;107(6):1604-1609. [PMID: 7781354](#). [Full Text](#)  
The criteria of Light et al remain the best method for distinguishing exudates from transudates. The serum-effusion albumin gradient is useful when patients are receiving concurrent diuretic therapy.
- <sup>4</sup> Heffner JE, Brown LK, Barbieri CA. Diagnostic value of tests that discriminate between exudative and transudative pleural effusions. *Chest*. 1997;111(4):970-980. [PMID: 9106577](#). [Full Text](#)  
Meta-analysis of studies that report the diagnostic value of pleural fluid tests.
- <sup>5</sup> Prakash UB, Reiman HM. Comparison of needle biopsy with cytologic analysis for the evaluation of pleural effusion: analysis of 414 cases. *Mayo Clinic Proceedings*. 1985;60(3):158-164. [PMID: 3974296](#).

This study shows that cytologic analysis has a higher sensitivity than needle biopsy for diagnosing malignant pleural effusions. The value of needle biopsy is limited in establishing the cause of pleural effusion that results from either malignant or nonmalignant disease, with the exception of tuberculous pleurisy.

- <sup>6</sup> Antunes G, Neville E, Duffy J, Ali N. BTS Guidelines for the management of malignant pleural effusions. *Thorax*. 2003;58:ii29-38. [PMID: 12728148](#). [Full Text](#)

This article provides guidelines for the management of malignant pleural effusions.

- <sup>7</sup> Clementsen P, evald T, Grode G, et al. Treatment of malignant pleural effusion: pleurodesis using a small percutaneous catheter. A prospective randomized study. *Respiratory Medicine*. 1998;92(3):593-596. [PMID: 9692129](#).

This prospective randomized study concluded that pleurodesis in patients with recurrent malignant pleural effusion can be performed with a small percutaneous catheter (Cystofix) with an effect similar to that obtained with a large-bore chest tube and with less discomfort for the patient.

- <sup>8</sup> Brega-Massone PP, Lequaglie C, et al. Chemical Pleurodesis to Improve Patients' Quality of Life in the Management of Malignant Pleural Effusions: The 15 Year Experience of the National Cancer Institute of Milan. *Surg Laparosc Endosc Percutan Tech*. 2004;14(2):73-79. [PMID: 15287604](#).

This 15 year experience of the Milan NCI indicates that chemical pleurodesis represents a good palliative treatment of neoplastic pleural effusion. Talc pleurodesis by VATS is recommended as the choice treatment in case of recurrent pleural effusions.

- <sup>9</sup> Shaw P, Agarwal R. Pleurodesis for malignant pleural effusions. *Cochrane Database Syst Rev*. 2004;(1):CD002916. [PMID: 14973997](#).

A review and meta-analysis of randomized controlled studies of talc as the sclerosant of choice, and thoroscopic pleurodesis as the preferred technique for pleurodesis based on efficacy.

- <sup>10</sup> Putnam JB Jr, Light RW, et al. A randomized comparison of indwelling pleural catheter and doxycycline pleurodesis in the management of malignant pleural effusions. *Cancer*. 1999;86(10):1992-1999.

144 patients (61 men and 83 women) were randomized in a 2:1 distribution to either an indwelling pleural catheter or doxycycline pleurodesis. The median hospitalization time was 1.0 day for the catheter group and 6.5 days for the doxycycline group. The degree of symptomatic improvement in dyspnea and the quality of life was comparable in each group.