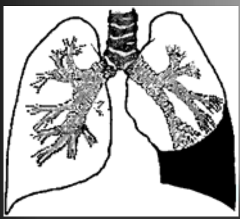
International Pleural Newsletter



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Use of Pleural Manometry

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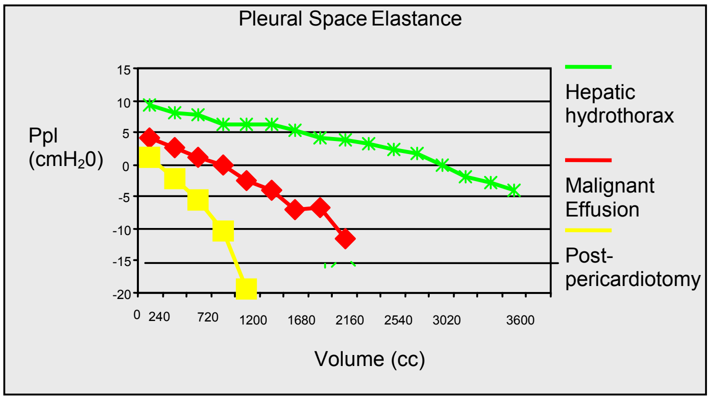
Although Quincke, in 1878, was the first to measure intrapleural pressure (Ppl) during the removal of pleural fluid[1], pleural manometry has only recently become a clinically important part of thoracentesis.

At functional residual capacity (FRC) Ppl is approximately -3 to -5 cmH$_2$0. Depending on the cause of the effusion, as fluid builds up in the pleural space, Ppl typically rises, and as the effusion is removed, the lung should expand, the chest wall contract and the Ppl reach its steady-state at FRC. Pleural pressure, however, can be negative, as in the case of trapped lung, or start out positive, and drop suddenly as is the case with lung entrapment. Trapped lung results from prior pleural inflammation causing visceral pleural scarring and produces an effusion ex-vacuo, with the fluid being transudative. Lung entrapment, however, describes an inability of the lung to re-expand due to visceral pleural thickening, endobronchial obstruction, or increased elastic recoil of the lung from interstitial disease such as lymphangitic carcinomatosis.

During a thoracentesis as much fluid as possible should be removed with the goals of maximizing symptomatic relief and sparing the patient multiple procedures. Furthermore, other diagnostic tests, such as a post-thoracentesis CT scan, are much more valuable when the pleural space is 'dry'. Pleural manometry allows for the safe drainage of large volumes of fluid as well as avoiding the pressure-related consequences of thoracentesis such as re-expansion pulmonary edema.

In 1980, Light and colleagues used a U-shaped manometer to measure mean pleural pressure during thoracenteses in 52 patients[2]. Though the initial Ppl varied widely (-21cmH$_2$0 to +8cmH$_2$0), an initial pressure of <-5cmH$_2$0 was only seen with malignant effusions or trapped lungs. Three distinct pleural elastance curves were described: 1) removal of a large amount of fluid with minimal change in pressure, 2) a relatively normal initial curve followed by a sharp drop in pressure, and 3) a negative initial pressure with a rapid drop in pressure (fig.1 shows data from our institution illustrating these curves). Furthermore, their study showed that if thoracenteses were terminated when the Ppl dropped to <-20 cmH_20, re-expansion pulmonary edema was avoided despite removing large quantities of fluid.



For pleurodesis to be successful, the pleural surfaces need to appose each other. If the lung is entrapped and does not re-expand during thoracentesis the odds of successful pleurodesis are reduced. Lan and colleagues found a pleural space elastance of $\geq$19cmH_20/500mL predicted pleurodesis failure[3]. This is clinically useful, as these patients can still achieve palliation by placement of a chronic indwelling catheter, *eg* PleurX™ (Denver Biomed, Denver, CO, USA). Villena *et al* also found pleural elastance to be an excellent predictor of trapped lung[4].

In addition to the simple U-shaped manometer described by Light, Ppl can be measured using an overdamped water manometer or an electronic transducer system, and the benefits of each are nicely reviewed by Doelken *et al*[5].

In conclusion, pleural manometry provides a better understanding of the underlying pathophysiology, allows complete drainage during thoracentesis, and is a useful tool to select patients for pleurodesis or PleurX™ catheter placement. Though currently underutilized, the importance of pleural manometry is gaining momentum.

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Pulmonologist-Operated Pleural Ultrasound
Advantages and Training Recommendations

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The last 10 years have seen rising interest among pulmonologists in the use of pleural ultrasound. Ultrasound is safe, relatively inexpensive and allows real time visualization of pleural pathology. This allows immediate decisions to be made regarding appropriate management. Ultrasound machines suitable for pleural imaging now weigh as little as 3kg. This lends its use both in the outpatient setting as well as at the bedside. This is particularly important in critically ill patients on respiratory support.

Ultrasound is superior to radiographs for detecting pneumothoraces. When performed by pulmonologists sensitivities of 95-100% can be achieved - figures comparable to ultrasound performed by radiologists[1,2].

Historically, pleural biopsies were performed blindly by pulmonologists with low diagnostic yields for neoplastic disease. More recently, the utilization of ultrasound by pulmonologists to demonstrate pleural masses and assist percutaneous biopsy have shown promising results with sensitivities of 100% for mesothelioma and 85% for metastatic malignancies[3].

Furthermore, when chest x-ray findings are atypical for a pleural effusion, ultrasound can quickly differentiate pleural thickening from an effusion. If a small or multiloculated pleural effusion is demonstrated, thoracentesis can be safely and confidently performed with a low incidence of complications[4]. Alternatively, ultrasound may demonstrate a cause for the effusion, such as pleural thickening or diaphragmatic nodularity and a more appropriate site for aspiration.

Demonstration of a pleural effusion is relatively straightforward and requires minimal training. Imaging of complex pleural disease and guiding interventional procedures are more operator-dependent and require more focused and dedicated training. It is not a question of *who* should be performing pleural ultrasound but whether they are adequately trained, aware of their limitations and ensure their skills are maintained.

The European Federation of Ultrasound Societies in Medicine and Biology has recently highlighted the need for guidelines and proposed pan-European recommendations for the minimal training necessary to practice ultrasound[5].

Based on these recommendations the Royal College of Radiologists (UK) recently published guidelines for ultrasound training by medical and surgical specialties.

These guidelines encompass theoretical, technical and practical training in core aspects of thoracic ultrasound[6].

Level 1 skills equate to the minimum training necessary for a chest resident to perform and interpret common examinations proficiently and independently. This would require observing 20 ultrasound examinations, followed by performing supervised ultrasound examinations on 10 patients with a pleural effusion and on 20 normal subjects. The trainee should perform a minimum of five thoracenteses using both guided and non-guided techniques. **Level 2** skills equate to sub-specialty thoracic imaging training and require a minimum 100 thoracic ultrasound examinations covering a diverse range of pleural diseases and more complex guided interventional techniques. **Level 3** equates to the standard reached by a specialist thoracic radiologist.

Level 1 training would be possible both in teaching and non-teaching hospital settings. Level 2 and 3 training would only be possible in teaching hospitals with a dedicated thoracic radiologist. To ensure that skills are maintained, a minimum of 20 ultrasound scans per year should be performed with no more than three months between consecutive examinations.

Pulmonologists already possess knowledge of pleural anatomy and skills in pleural intervention. Training in pleural ultrasound would be a natural extension of these skills. This would enable pulmonologists to offer a more complete one-stop chest service and decrease potential delays in decision making and patient management.

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Pleural Effusion from Cerebrospinal Fluid (CSF) Leak

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A duro-pleural fistula (DPF), also termed subarachnoid pleural fistula, describes a communication between the subarachnoid and pleural spaces allowing CSF to accumulate in the pleural cavity. In its pure form the fluid is a transudate, because of the low protein of CSF.

Pathogenesis: For a DPF to develop there must be disruption of both the dural and pleural membranes allowing the development of a tract between the two spaces. A pressure gradient allows CSF to flow from the positive pressure subarachnoid space to the negative pressure pleural space.

Causes**:** A DPF is most commonly caused by blunt and penetrating trauma, with a total of 23 reports since 1959. This traumatic fistula can be caused by a missile transversing both the pleural and subarachnoid spaces or a vertebral fracture that tears the dura and parietal pleura. It has rarely been described following laminectomy. However, neurosurgical procedures may be a more common cause than trauma, as these DPFs may be recognized early and repaired without generating reports in the literature.

Clinical Features**:** A high clinical suspicion is required to establish the diagnosis. Postural headache, nausea, and vomiting should suggest a CSF leak. Symptoms related to the effusion, such as dyspnea, may be minimal or overshadowed by concomitant injuries, often delaying the diagnosis. Other clues to the diagnosis may include pneumocephalus or meningitis.

Chest x-rays may initially be normal. Effusions range from small to massive, depending on the size and duration of the fistula. Mediastinal widening may occasionally be seen.

The clinician should suspect a non-traumatic duro-pleural fistula on gross examination of the pleural fluid which 'looks like water'. The nucleated cell count is low and the pleural fluid glucose value is less than the serum value but not < 0.5mg/dL. An important feature of this transudative effusion is that the total protein is virtually always <1g/dL with the LDH clearly in the transudative range. Beta$_2$-transferrin, produced by neuraminidase activity in the brain, is found uniquely in the CSF and inner ear perilymph. This protein is accepted as a sensitive and specific marker to identify CSF leaks into the pleural space following head or spinal surgery. In the setting of trauma, the pleural fluid may be an exudate due to concomitant hemothorax or parapneumonic effusion.

Location of the DPF**:** Definitive identification of a DPF requires radiographic visualization. Conventional myelography and radionuclide myelography are most commonly used. Isotope myelography is more sensitive than the conventional study. A CT scan with myelography may be necessary to define a DPF with a slow or intermittent leak.

Management**:** Spontaneous resolution is rare and most patients require either surgical ligation or closed chest tube drainage. The appropriate timing of surgical intervention is unknown. Some advocate chest tube drainage for up to 2 weeks before surgical intervention, while others recommend early intervention.

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Challenges in Pleural Disease Management in Central America

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Pleural disease was the theme of the XIX Central American & Caribbean Pulmonary and Thoracic Surgery Congress for 2005 held in Guatemala. Representatives from participating countries presented audits from selected institutes of their countries, which provided insight to the common challenges in the management of pleural diseases in the region. Parapneumonic effusions, malignant effusions, and TB were the commonest types of exudative effusions.

Parapneumonic effusions were Gram stain positive in <35% of cases and culture positive in 15%, with *S. pneumoniae, S. aureus* and *K. pneumoniae* being the most common organisms. In the majority of countries, pH measurement in pleural fluid was under-utilized, as most laboratory personnel were concerned that (infective) pleural fluids may cause malfunction of the machine.

Patients with parapneumonic effusions often presented late: 90% of empyema patients presented >30 days after symptom onset. This delay of 1-2 months in presentation likely explained the prolonged hospitalizations (average 24 days) and the high portion (30%) of empyema patients that required surgical intervention[1]. Fibrinolytics were used only in Panama for empyema but not in other countries due to their costs and the conflicting data on its effectiveness[2,3].

For infective effusions (parapneumonic, empyema and TB), 90% resolved with therapeutic thoracentesis plus antimicrobials. Large bore chest tube was placed in 34% of patients with the majority of cases utilizing a single bottle collection system without suction. Decortication was the surgical procedure of choice, with most of the cases being pediatric patients, since video-assisted thoracoscopy (VATS) is seldom practiced in this age group in our region.

Malignant effusion was the second most frequent cause of effusions: primary lung adenocarcinoma was the most common histology, followed by breast cancer. The majority of effusions were exudates. Pleural fluid pH was seldom obtained as they rarely influence clinical decisions[4]. Therapy involved chemotherapy plus: therapeutic thoracentesis (25-57% among different countries), chest tube drainage (40-75%) and pleurodesis (30-43%). Access to pleurodesis agents was a problem leading to a variety of compounds used depending on local availability (table 1). In particular, sterilized talc is unavailable in many centers. As human grade tetracycline is no longer marketed, many physicians resort to veterinarian tetracycline preparations. Utilization of surgical pleurodesis varied: VATS with pleurectomy was performed in 15% of cases in Guatemala but only rarely in Nicaragua. In the Guatemala audit, decortication was performed in three cases with a 67% post-operative mortality rate. The majority of patients were then referred to the oncologists for follow-up.

	Guatemala	Nicaragua	Panama	Venezuela
Talc Slurry	83%	0%	0%	22%
Veterinarian tetracycline	17%	0%	0%	56%
Bleomycin	0%	17%	0%	11%
Methotrexate	0%	25%	0%	0%
Depomedrol	0%	0%	0%	11%
Iodopovidine	0%	58%	100%	0%

Table 1: *Pleurodesing agent audit as reported by country representatives at the Central Amercian & Caribbean Pulmonary Congress in 2005. El Salvador, Honduras and Costa Rica did not report on the frequency of their use of pleurodesing agents.*

TB pleuritis was diagnosis by Ziehl-Neelsen-staining (5%), cultures (5%) or pleural biopsy (63%). Only Panama and Honduras have access to adenosine deaminase (ADA) testing to aid diagnosis of TB effusion[5]. Most patients presented >30 days after symptoms began. Consequently, 20% required surgical intervention with high morbidity (*eg* bronchopleural fistula, sepsis) and long hospitalizations.

In conclusion, pleural diseases are common in Central America. Despite the lack of diagnostic tools (fluid pH, ADA levels), limited access to suction compatible collecting systems, and difficulty in obtaining sterilized talc or tetracycline for pleurodesis, treatment success rates remain comparable with published data in the literature.

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Adenomatoid Tumor of the Pleura:
A Case Report

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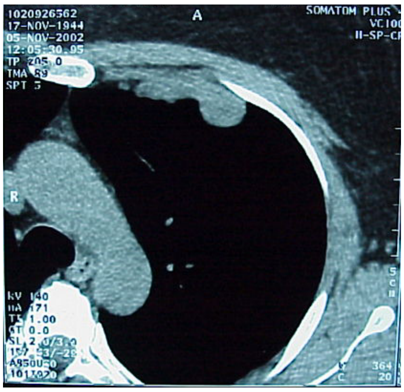
A 58 year-old woman had a routine chest film which was abnormal. CT scan showed a left thoracic wall lesion with soft tissue density and low contrast concentration.

CT guided biopsy showed a lesion formed by acini of vacuolated cuboid cells which were immuno-reactive against AE1/AE3 and calretinin, consistent with an adenomatoid tumor.

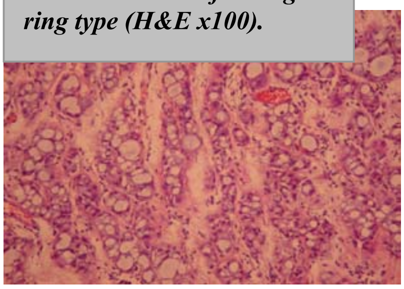


The patient had no other systemic lesions. A left thoracotomy revealed a 2.8 x 2.6 x 1.3 cm tumor which was removed by pleurectomy. The lung and the mediastinal structures were not involved. The patient was discharged three days later in excellent conditions. The histopathologic examination of the nodule confirmed an adenomatoid tumor of the pleura.

Adenomatoid tumors are benign neoplasms found predominantly in genital tracts. Despite the abundance of mesothelial cells in the pleura, adenomatoid tumors are apparently extremely rare in this location and only a few cases of pleural origin have been reported.

Considered as a benign variant of mesothelioma, adenomatoid tumors contain plump acidophilic, frequently vacuolated cells organized in tubules and cords within a fibrous stroma. Despite their characteristic mesothelial phenotype and histological appearance, adenomatoid tumors have an extensive list of differential diagnoses that includes vascular neoplasm, germ cell tumor, metastatic adenocarcinomas, and malignant mesothelioma.

Tumor showing tubules, microcysts lined by flat cells and cords formed by vacuolated cells of the signet ring type (H&E x100).



Urinothorax:
A Case Report

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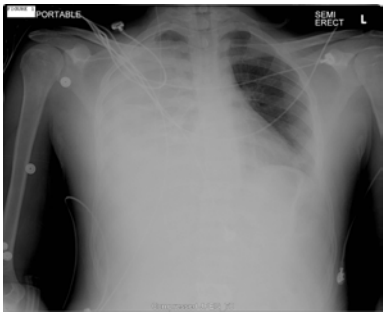
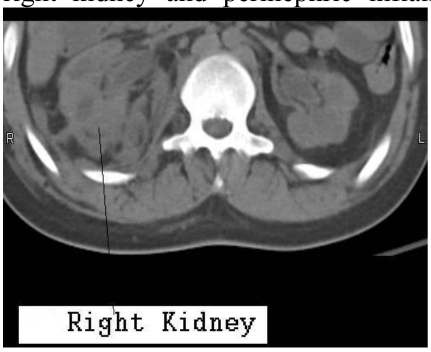
Urinothorax is urine in the pleural space. This fluid is usually a transudate with low pH. We report a case of urinothorax with an exudative effusion.

A 24 year old male presented with complaints of decreased urine output and cloudy urine. He had a history of spina bifida and neurogenic bladder. Urinalysis showed numerous leukocytes and cultures grew Proteus mirabilis. A chest film revealed a right pleural effusion.



His pleural fluid revealed a LDH level of 1450 IU, protein of 4.2g/dL, and creatinine of 3.3mg/dL (serum creatinine 2.7mg/dL).

CT scan showed emphysematous pyelonephritis of the right kidney and perinephric inflammatory changes. The patient underwent radical right nephrectomy. Right-sided decortication was later performed as chest tube drainage was not adequate. His clinical condition improved and was discharged.



Urinothorax occurs when urine leaks into the retroperitoneum, and migrates transdiaphragmatically into the pleural cavity. It is usually seen with urinary obstruction. Diagnosis of urinothorax is made by finding a creatinine level in the pleural fluid higher than simultaneously measured serum creatinine. The pleural fluid in urinothorax is classically described as a transudate, as defined by Light's criteria. Our patient had an exudate, which may be due to active infection of the pleural space by the organisms from the urine.

If you have any comment on the Newsletter or any interesting cases of pleural disease, contact:
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