International Pleural Newsletter

A Publication of the International Pleural Network

Volume 6 Issue 4
October 2008

Pleural Fluid pH: the Acid Test

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The pleural literature and practice guidelines[1] have emphasized the usefulness of measurement of the pH of pleural fluids in the workup of pleural effusions. Acidic pH (<7.20) in parapneumonic effusions is often taken as the cutoff for need of chest tube drainage[2]. In malignant effusions, pleural pH is a reflection of the load and metabolic activity of pleural tumors: a low pH is associated with poorer survival and unsuccessful pleurodesis[3]. However, the usefulness of pleural pH depends on accurate measurement protocols. Clinicians need to be aware of the limitations of the test.

A recent study suggests that in loculated effusions, the pH in different locules (within the same patient) may vary: in 3 of the 7 patients, the variation in pH was sufficient to alter clinical practice[4].

How pH is measured matters: pH meters and litmus papers have been shown to be inaccurate, and blood gas machines should be used to assess pleural fluid pH.

The devil is in the detail. The collection method of pleural fluid can also significantly alter the pH measurements. Recent data showed that presence of air in the collection syringe artificially raises the pH significantly (median rise=0.08)[5]. This is likely a result of rapid diffusion of CO_2 from pleural fluid (usually several kPa in magnitude) to atmospheric air.

Most patients undergoing thoracentesis will receive local anesthesia, especially lidocaine. The pH was lower if the pleural fluid was collected after tissue infiltration of lidocaine[6]. To further prove the point, Rahman *et al* has shown that residual lidocaine as little as 0.2mL (approximately the dead space of a

22G needle) could decrease the pH by a median value of 0.15. The more the residual lidocaine, the greater was the reduction in pleural fluid pH[5]. This is presumably because of the very acidic pH of lidocaine (pH~6). Interestingly, presence of heparin (also acidic) induces only a minor (and clinically insignificant) reduction in pleural fluid pH[5, 7].

Once collected, the pleural fluid should be analyzed within one hour[5, 8]: changes in pH - can be either increase or decrease - will occur with further delays[5]. Many factors can alter the pH. In addition to CO_2 shift, pleural fluid contents (eg hyaluronic acid) and metabolic products from inflammatory and mesothelial cells, and (if present) cancer cells and bacteria all contribute.

Glucose in pleural fluid has been suggested as an alternative to pH, and can generally provide similar clinical information. Its quantification is less vulnerable to collection or processing irregularities (presence of air and lidocaine etc) and is stable at room temperature for at least 24 hours[5]. Glucose quantification can be obtained at the point-of-care, eg using blood gas analyzers, and should be considered as a legitimate alternative to pH measurement. In the meantime, a standardized method of pleural fluid collection for pH measurement is needed.

1. Maskell NA, et al. Thorax 2003; 58 Suppl 2:ii8-17
2. Heffner JE, et al. Am J Respir Crit Care Med 1995; 151:1700-8
3. Davies HE, et al. In: Light RW and Lee YCG, eds. *Textbook of Pleural Diseases*, 2nd ed., pp. 569-582. London, 2008.
4. Maskell NA, et al. Chest 2004; 126:2022-4.
5. Rahman NM, et al. Am J Respir Crit Care Med 2008; 178:483-90.
6. Jiménez Castro D, et al. Chest 1999; 116:399-402.
7. Bou-Khalil PK, et al. Respiration 2007; 74:659-62.
8. Sarodia BD, et al. Chest 2000; 117:1043-8.

What is new in Imaging of Malignant Pleural Mesothelioma (MPM)?

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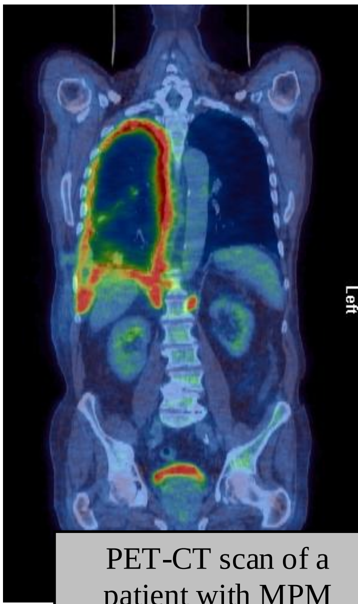
Advances in chemotherapy for MPM have led to a renewed interest in finding the best imaging techniques to detect and predict disease response. Three methods currently show the most promise: Positron emission tomography with ^{18}fluorodeoxy-glucose (^{18}FDG-PET), dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) and quantitative volumetric computed tomography (CT).



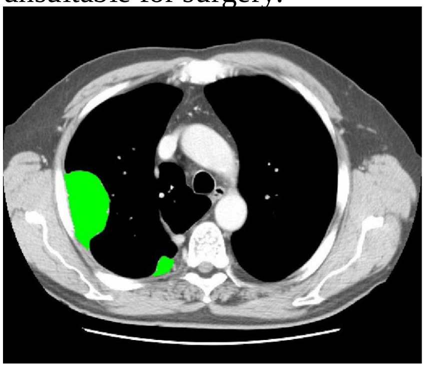
PET-CT scan of a patient with MPM

^{18}FDG-PET provides a measure of glucose uptake within tissues and thus their metabolic activity. In MPM, PET is a useful adjunct for staging and its potential to predict prognosis and response to chemotherapy is being explored. MPM patients whose tumors had a high maximum standardized uptake value (SUVmax; cut-off 4.03) had a 12-month survival of 17% compared with 86% for the low SUVmax group[1]. Flores et al[2] divided 137 MPM patients into high and low SUV groups (using a SUVmax cut-off of 10). The median survival was 21 months in the low SUV group and 9 months in the high SUV group. In 20 patients undergoing chemotherapy containing pemetrexed, those who experienced a metabolic response (defined by 25% or more in reduction in SUV) had a significantly longer time to tumor progression and a trend towards longer overall survival[3].

Francis et al[4] have demonstrated the potential of total glycolytic volume (TGV) for measurement of early disease response in MPM. This semi-quantitative measurement is calculated by defining a volume of interest on the PET scan. In 20 patients who underwent PET and CT, a fall in TGV after one cycle of chemotherapy significantly correlated with improved patient survival whereas changes in SUVmax and CT measurements (modified RECIST criteria) were not.

DCE-MRI involves repeatedly imaging the same anatomical area following injection of gadolinium contrast media. The uptake of contrast in the tissue and subsequent washout allows calculation of several pharmacokinetic parameters that reflect tumor perfusion, vascularity and vascular permeability. This technique has been extensively studied in other tumors such as breast, brain and primary lung cancer but has only recently been used in MPM. In 19 patients undergoing chemotherapy for MPM, the redistribution constant (one of the pharmacokinetic parameters) correlated well with tumor response to chemotherapy and survival[5]. Confirmation in larger studies is needed.

Previous studies have shown that clinical response to chemotherapy has not always correlated with CT findings. This may be partly due to the lack of a suitable measurement of the volume of a tumor which tends to grow in a circumferential manner. One option is to measure the entire volume of disease within the thorax, eg using automated computerized programs. Alternatively, Pass et al[6] used a manual segmentation method in 47 patients undergoing surgery for MPM. CT derived pre-operative volume was compared with the volume of the resected specimen and overall survival. They showed that both pre-operative and specimen volume measurements correlated with survival. This method requires validation in patients with larger tumor volumes unsuitable for surgery.



Segmentation of MPM (in green) on CT using a semi-automated computer algorithm

The role of the above-mentioned techniques will become clearer through clinical trials and may aid determination of prognosis and treatment response in future.

1. Benard F, et al. J Nucl Med 1999; 40: 1241-5.
2. Flores RM, et al. J Thorac Cardiovasc Surg 2006; 132:763-8.
3. Ceresoli GL, et al. J Clin Oncol 2006; 24:4587-93.
4. Francis RJ, et al. J Nucl Med 2007; 48:1449-58.
5. Giesel FL, et al. Chest 2006; 129:1570-6.
6. Pass HI, et al. J Thorac Cardiovasc Surg 1998; 115; 310-8.

If you have any comment on the Newsletter or interesting cases of pleural disease, contact: Ms Emma Hedley ***emma.hedley@orh.nhs.uk***

What is new in Pneumothorax?

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Primary spontaneous pneumothorax (PSP) remains a significant global health problem. Controversies continue to surround its pathophysiology and management.

PSP occurs, by definition, in patients without underlying lung disease. Many studies have suggested that rupture of blebs may be the cause of pneumothorax. Much of this evidence is circumstantial and a causal link has yet to be proven. Blebs may not be as important as previously thought.

A recent study[1] suggests that pleural porosity, rather than blebs or bullae, is the main cause for PSP. Pleural abnormalities found at white light thoracoscopy (anthracosis, cobblestone malformation, blebs, bullae) are more common in patients with PSP, but are also present in healthy controls. However, Fluorescein-Enhanced Autofluorescence Thoraco-scopy (FEAT) revealed “hot spots” or large areas of subpleural fluorescence only in those with PSP and in areas that appeared normal under white light. This study raises questions about the relevance of visible blebs and suggests that high-grade pleural lesions under FEAT could be representative of pleural porosity.

Pleural porosity is the presence of pleural pores several microns in diameter. The exact relevance of this porosity is unknown and may be due to the loss of surface mesothelial cells, thinning and rupture of the basement membrane or down regulation of junctional proteins. Further study is required as the site of an air leak has an impact on recurrence management.

The literature shows that the management of PSP is variable and guideline adherence poor. Guidelines from the British Thoracic Society[2] and American College of Chest Physicians (ACCP)[3] agree that in patients who are clinically stable with a small pneumothorax, observation alone may be appropriate.

The guidelines differ on the use of simple aspiration as the first intervention in those patients who have a large symptomatic pneumothorax. However, since the publication of the ACCP guidelines, further evidence has been produced confirming that simple aspiration[4] has a similar success rate to intercostal tube drainage and is a less invasive and more economical approach.

If simple aspiration fails, what do we do next? The literature suggests several options, none of which have been compared in head to head trials. One simple approach likely to become popular is small catheter aspiration followed by attachment to an underwater seal or an integral one-way valve system that will allow out patient management. The alternative is insertion of a standard intercostal drain which requires an inpatient stay.

Outpatient management with a small caliber catheter and one way valve is an attractive alternative which has had its advocates since the 1970's[5]. This approach has been revisited recently and shown to be safe[6].

Should we recommend a thoracoscopic approach as a definitive treatment following failed aspiration of a first PSP? This may offer fewer complications and a shorter hospital stay[7], although a randomized controlled trial is needed first.

For a first recurrence however, most physicians would now recommend video assisted thoracoscopic surgery (VATS) with bullectomy and pleural abrasion to deal with the underlying pleural porosities. The role of poudrage with large particle calibrated talc is uncertain, and whilst safe and effective has not been compared to VATS techniques in a trial setting.

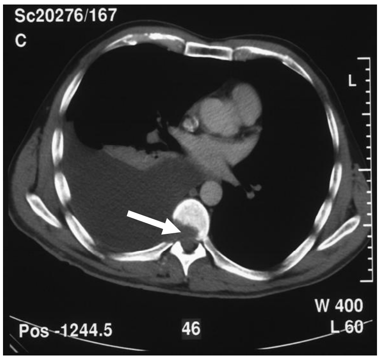
On a lighter note, new research has shown that patients with PSP have higher anger levels than controls[8]. In conjunction with loud music inducing PSP[9], perhaps heavy metal rock concerts should now come with a health warning!

1. Noppen M, et al. Am J Respir Crit Care Med 2006; 174:26-30.
2. Henry M, et al. Thorax 2003; 58:ii39.
3. Baumann MH, et al. Chest 2001; 119:590-602.
4. Noppen M, et al. Am J Respir Crit Care Med 2002; 165: 1240–4.
5. Page A, et al. Can Med Assoc J 1975; 112:707-9.
6. Choi SH et al. Eur J Cardiothorac Surg 2007; 31: 491-5.
7. Chen JS, et al. Ann Thorac Surg 2008; 85: 1908-1913.
8. Lee SH, et al. Gen Hosp Psych 2008; 30: 331-6.
9. Noppen M, et al. Thorax 2004; 59:722-4.

IMAGES OF THE PLEURA

A Pleural Effusion Following Thoracic Discectomy

A 44 year old man with myelopathy and bladder disturbance underwent a right transthoracic T7/8 discectomy for a large calcified disc. Post-operatively



he developed mild breathlessness and headaches. A right-sided pleural effusion was evident on the chest radiograph and a CT scan showed continuity with the sub-arachnoid space at T7/8 (left).

The effusion was drained. The fluid was a transudate, and was positive for beta-2 transferrin, confirming the presence of cerebrospinal fluid (CSF) from a duro-pleural fistula.

The effusion resolved with conservative management, and a myelogram eight weeks post-operatively (right) demonstrated a thoracic pseudomeningocele with no leak of contrast into the pleural cavity.

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Educational Programs on Chest Tube Insertion and Management: The Queensland Experience

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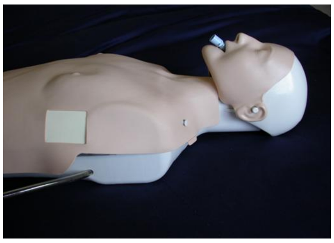
Adverse events related to insertion and management of chest tubes can result in significant morbidity and mortality as well as large payouts in compensation and legal costs. The Queensland Intercostal Catheter Collaborative (QICC) was established in 2003 in response to a request from the Thoracic Society of Australia & New Zealand (TSANZ) to standardize procedures/protocols and to develop education material relating to chest drains. The QICC involves multi-disciplinary medical and nursing practitioners from Queensland, New Zealand, the UK and Canada.

Innovative educational programs, combining e-learning and practical skills in a simulation environment have been developed for doctors and nurses. The program is evidence-based where evidence exists. Otherwise, consensus is drawn from international and national guidelines. Information related to 'real-life' problems has been gained through structured interviews[1], audits, surveys and focus groups. Our data indicate that, unlike a decade ago, junior doctors are frequently unable to get practical experience in chest tube insertion and many fellows (≥4 years post graduation) have no experience in the procedure.

> The online programs – *Insertion of chest tubes and management of chest drains in adults* for doctors and nurses and audit tools can be accessed at http://www.thoracic.org.au/glchestdrain.html.
> Free access to the program will be available from December 2008 at www.safetyandquality.gov.au

The web-based medical education in relation to insertion and management of chest drains in adult patients is recommended for junior or inexperienced doctors. It consists of a flexible program of up to 3 hours using evidence-based educational interventions and human factors theory[1] encompassing anatomy, physiology, risk assessment, procedures and management of difficult cases. Prior to simulation training, it is recommended that all intending trainees pass a short quiz to show adequate anatomical and procedural knowledge and complete the module 'Assessing risk and minimizing complications in chest tube insertion'.

Practical skill training employs a mannequin simulator (see www.simcentral.com.au) which has a ribcage and a multi-layered pad in each lateral chest wall. This allows simulated practice of chest tube insertion under the guidance of an experienced clinician. Manuals are available on-line and include a matrix of risks that can affect the outcome of the procedure.



Depending on the experience of the trainee, scenarios of varying complexity containing mitigatable and non-mitigatable risks can be constructed. The simulator can also be used with an underwater seal chest drain for scenarios designed to demonstrate the management and trouble shooting of chest drains. The nursing program is similar in design with emphasis on the nursing role as part of the procedural team.

Compared to traditional educational formats, there is evidence that e-learning, especially if interactive, can improve knowledge transfer[2], sustainability of intervention effects[3] and is preferred by students[2, 3]. Training for chest tube insertion on the same mannequin following a brief didactic teaching session is also effective[4]. Assessment of clinical outcomes can be problematic. Reported incidents increase after training due to better reporting and cannot be used as a reliable outcome measure. Chart review[2] and routine auditing (see Audit Tools on-line) are time consuming, but may identify deviations from accepted practice.

For junior doctors this combined approach allows assessment of knowledge, risk awareness and manual skills before supervised chest drain insertion is attempted in a patient, potentially reducing patient discomfort and adverse outcomes. Assessment using complex scenarios can be used to assess competence for more senior doctors.

1. Joughin KE. PhD dissertation: Queensland University, 2007.
2. Wutoh R, et al. J Contin Educ in Health Prof 2004; 24:20-30.
3. Fotheringham MJ, et al. Am J Prev Med 2000; 19:113-20.
4. Hutton IA, et al. Intern Med J (in press).

Funding declaration: Queensland Health, Med-E-Serv, TSANZ