Pleural fluid myths and elusive effusions

James Goldring
Pleural fluid appearances

What proportion of transudates are turbid?
• 9%

What proportion of MPE are bloody?
• 11%

(47% of bloody effusions are MPE)

Chylothorax

Chylothorax is milky?

- Serous: 26%, serosanguinuous 26%, bloody 3%
- 14% have triglycerides <1.2mmol/L
- Depends what you eat
- If in doubt check for chylomicrons with lipoprotein electrophoresis

Optimal quantity (mls) for cytology

• There is no point in sending >50mls for cytology?

50ml vs the remainder 55% regardless


Depends on what your lab does with it:

10mls 49% 60mls 63% 150mls 69% (if doing **cell block** as well as smear/cytospin)

Swiderek J et al. Prospective study to determine the volume of pleural fluid required to diagnose malignancy. *Chest* 2010;137:68
Delays in sending sample

• Pleural fluid should be analysed asap?

Cytology (incl IHC, genotyping) 14d refrigerated

Glucose 24hrs

Cell differential 1d
Conner BD et al. Variations in pleural fluid WBC count and differential counts with different sample containers and different methods. *Chest* 2003;123:1181

pH 4hrs
Rahman NM (2008)
Light’s criteria

• Light’s criteria is the best method for separating transudates from exudates?

Light’s criteria 98% sensitive, 74% specific
Requires serum sampling (up to 5d later)


Single tests improve specificity (pleural protein >30g/L 92% sensitive, 83% specific)

Heffner JE et al. Diagnostic value of tests that discriminate between exudative and transudative pleural effusions. Chest 1997; 111:970
Misclassification of transudates

- 30% of CCF related effusions & 18% of hepatic hydrothoraces (HH) are misclassified by light’s criteria mostly because both chronicity and diuretic increase LDH & protein


- If you suspect CCF use albumin gradient (s.alb-p.alb>12g/L) will correctly identify 83% of “false” exudates

- for HH use the albumin ratio (p.alb/s.alb<0.6) will correctly identify 78% of the “false” exudates

- Or the protein gradient (s.pr-p.pr) > 31g/L will correctly identify 55% of CCF and 61% of HH

  Bielsa et al. Solving the light’s criteria misclassification rate of cardiac and hepatic transudates. *Respirology* 2012;17:721

Misclassification of CCF transudates and NT-proBNP

• Is serum NT-proBNP better than albumin gradients and protein gradients?

• Yes but only pleural NT-proBNP >1300pg/ml validated so far.


• Serum NT-proBNP >1500pg/ml usual cut off in trials

• Evidence for BNP is scarce

  BTS 2010 pleural guidelines
Protein/LDH discordance

- You only need 1 of Light’s criteria to make an exudate- much of the time the 2 or 3 tests are concordant but...
- If the protein is high and LDH low think of
  - 1. bloody tap
- 2. Chylothorax
- 3. Yellow nail syndrome

- If LDH high and protein low think of
  - 1. malignancy
  - 2. parapneumonic effusions
  - 3. PCP

- V high LDH (>1000IU): infection, rheumatoid, malignancy
- V high protein (> 70g/L): multiple myeloma, waldenstroms macroglobulinaemia
Investigation of unilateral pleural effusion

BTS 2010 pleural guidelines
Elusive effusions

• Despite work up approx 5-20% of effusions remain undiagnosed

• Aims
Exclude a treatable cause
Avoid unnecessary interventions
Exudate or transudate - use light’s criteria,

Think of uncommon causes: revisit history, examination, drug history

Reconsider thoracoscopy? LA

PE? d-dimer then CTPA

Abdo pathology? Subphrenic, chronic pancreatitis, ovarian

If clinical suspicion of CCF or HH use albumin or protein gradients

Tests: serum HIV, pleural lipids & amylase

High NT-proBNP? Treat for heart failure

Reconsider hepatic hydrothorax even if no ascites

Dialysis? Or Nephrotic syndrome

Test: serum TFTs

If no treatable cause found - watch & wait vs. interval scanning.
## Uncommon effusions

<table>
<thead>
<tr>
<th>Transudates</th>
<th>Exudates</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trapped lung (after initial inflammatory process)</td>
<td>Yellow nail syndrome</td>
</tr>
<tr>
<td>Constrictive pericarditis</td>
<td>Benign asbestos pleural effusion (BAPE)</td>
</tr>
<tr>
<td>Urinothorax</td>
<td>Fungal</td>
</tr>
<tr>
<td>Peritoneal dialysis</td>
<td>Connective tissue disease</td>
</tr>
<tr>
<td>SVC obstruction</td>
<td>Drugs</td>
</tr>
<tr>
<td>Mitral stenosis</td>
<td>Meigs</td>
</tr>
<tr>
<td></td>
<td>Lymphoma</td>
</tr>
<tr>
<td></td>
<td>Chylothorax</td>
</tr>
<tr>
<td></td>
<td>Post cardiac injury</td>
</tr>
</tbody>
</table>
Drug induced effusions

10-50 cases on pneumotox
- Nitrofurantoin
- Methotrexate (some eosinophilic)
- Amiodarone
- Bromocriptine
- Docetaxel
- Imatinib
- Clozapine
- Sodium valproate (eosinophilic)
- Isoniazid (ANA +)
- Anti-TNF
Pulmonary embolism as a cause of pleural effusion

- More common than we think - 4th leading cause
- Dyspnoea out of proportion to size of effusion
- 30% associated with effusion
- Only 5% in thoracocentesis series
- Usually unilateral and mostly just blunting of costophrenic angle
- Doesn’t usually persist beyond 3 weeks

“no cause found”: Idiopathic pleuritis


- 75 patients with a histological diagnosis of non-specific pleuritis.
- Age 63.4 (±13.3) yrs, Mean follow up 32.9 (±27.4) months
- 8.3% malignant (21.4% of patients with asbestos exposure compared to 4.3% of those without), 91.7% benign
- True idiopathic in 25% (15/60)

![Diagram](image)

**Fig. 1.** Evolution of patients with the histological diagnosis of non-specific pleuritis after thoracoscopy.
Truly idiopathic in 25%

- 2 cases of BAPE ultimately mesothelioma
- 3 cases of TB- lymphocytic exudate, +TST, contact- no clinical benefit seen
- Radiotherapy?
Summary

• Correct interpretation of pleural fluid analysis and a systematic approach to undetermined effusions enables diagnosis in most cases

• Most undiagnosed effusions turn out to be benign and self-limiting
IPC practical

- http://vimeopro.com/user26937648/rocketvideozone/video/91925239