State of the Art in Management of Challenging Pleural Effusions

Mājid Shafiq, MD MPH

Assistant Professor of Medicine

Medical Director, Interventional Pulmonology

Assistant Fellowship Director for Procedural Education

mshafiq@bwh.harvard.edu

BWH BRIGHAM AND WOMEN'S HOSPITAL | The Lung Center |

HARVARD MEDICAL SCHOOL

Disclosures

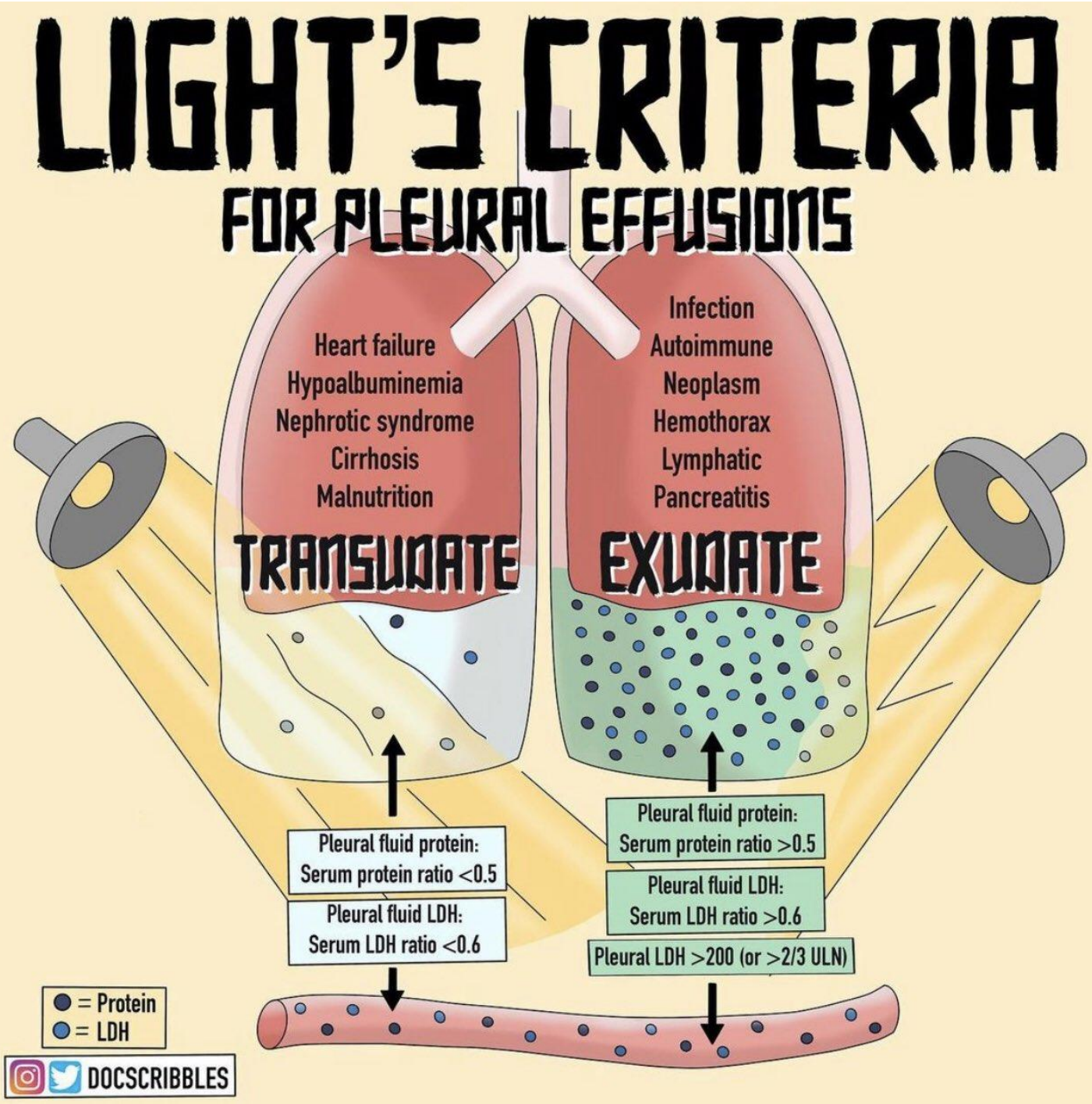
- Scientific Advisory Board
  - Ambu A/S (one of the manufacturers of single-use bronchoscopes)

Outline (learning objectives)

1. Working up **unexplained pleural exudates**
2. Managing **recurrent, symptomatic pleural effusions**
3. Managing **complicated pleural infections**

LIGHT'S CRITERIA

FOR PLEURAL EFFUSIONS



Working up an unexplained pleural exudate

- Definition of unexplained exudate:

When Light's criteria indicates an exudate and the clinical picture and additional labs (e.g., micro, cytology, flow cytometry) fail to definitively identify a cause

➢ 3 most common pearls to keep in mind:

Feller-Kopman D, Light R. NEJM 2018
Kassirian S, et al. Thorax 2023

1. Many transudates are falsely classified as exudates (pseudo-exudates)

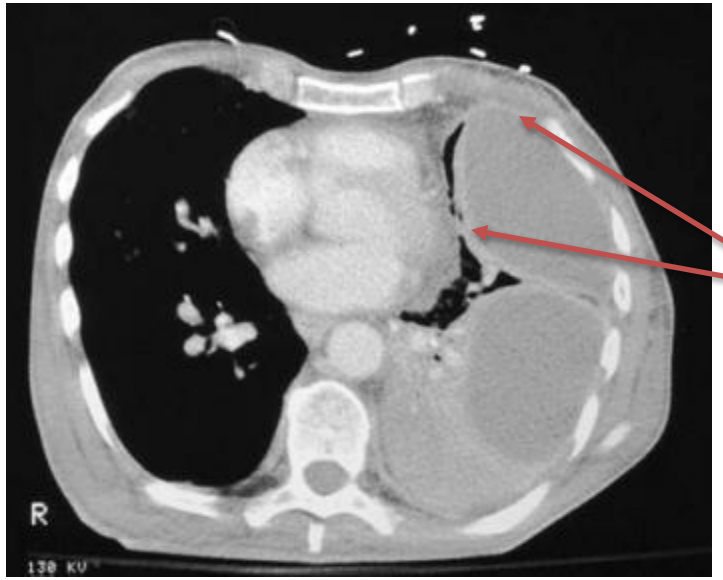
- Is the clinical picture fitting for a transudate?
  - PMH (CHF/cirrhosis/renal failure), exam (fluid overload), bilaterality, serum NT pro-BNP elevated?
- Did the patient recently receive diuretic therapy?
- Is the effusion responsive to diuretic therapy?
- Is the effusion exudative only per protein criteria?
  - No elevated LDH?
  - No neutrophilia?
  - Cholesterol levels <45mg/dl? (typically elevated in exudates)
  - Serum fluid albumin gradient > 1.2g/dl?

Bielsa S, et al. Respirology 2012
Feller-Kopman D, Light R. NEJM 2018

2. G stain and cultures are not great at catching infection

[approx. 50% sensitivity]

- Keep the entire clinical picture in mind when arriving at the presumptive diagnosis
- Imaging may show:
  - Concurrent pneumonia | Advanced cases: Split pleura sign and/or loculated effusion



Split pleura sign with enhancing and thickened and easily discernable pleural layers

2. G stain and cultures are not great at catching infection
[approx. 50% sensitivity]

- Keep the entire clinical picture in mind when arriving at the presumptive diagnosis
- Imaging may show:
  - Concurrent pneumonia | Advanced cases: Split pleura sign and/or loculated effusion
- Pleural fluid analysis may show:
  - ✓ Neutrophilic predominance (not always in subacute infection)
  - ✓ In advanced disease:
    - ❖ Low pH, glucose
    - ❖ Frank pus
    - ❖ (+) G stain or culture (±PCR; not widely available)
      - Negative G stain or culture DOES NOT rule out pleural infection

Maskell N, et al. NEJM 2005

3. Pleural fluid cytology is not great at catching malignancy [approx. 50-60% sensitivity]

- To ensure optimal pleural fluid cytology yield: Send at least 25ml! (BTS)
- Repeat pleural fluid cytology: Only modest ↑ in pooled sensitivity
- Pleural biopsy: Approx 95% sensitivity
  - Medical pleuroscopy (mod sedation, spontaneous breathing) vs. VATS (GA/ETT)
    - Similar safety profile and diagnostic performance
    - ↓ LOS and healthcare costs? [single-center study in Toronto; MP cases done outside of OR]

Roberts ME, et al. Thorax 2023
Shafiq M, et al. Chest 2020
McDonald CM, et al. Ann Thorac Surg 2018

Outline

1. Working up **unexplained pleural exudates**
2. Managing **recurrent, symptomatic pleural effusions**
3. Managing **complicated pleural infections**

Managing recurrent, symptomatic pleural effusion:

Options at hand

- OUTPATIENT OR INPATIENT: PRN thoracentesis
- INPATIENT: Chemical pleurodesis via chest tube (or thoracoscopically)
  - Talc poudrage introduced by Bethune in 1935
  - Contraindicated in case of incomplete lung expansion

Bethune, N. J Thorac Cardiovasc Surg, 1935

- OUTPATIENT: Tunneled, indwelling pleural catheters (IPCs)
  - FDA approval: 1997 | First RCT published: 1999

Putnam JB, et al. Cancer, 1999

- OUTPATIENT: IPC-Plus protocol (talc via IPC)

Bhatnagar, et al. N Engl J Med, 2018

Recurrent **malignant** pleural effusion:

Encouraging trends and need for improvement

- 2004 – 2014 NIS study: Shift to outpatient care, presumably 2/2 IPCs > pleurodesis
  - Annual hospitalizations: 38,865 -> 23,965
  - Median LOS: 7.7 days -> 6.3 days
  - Annual hospital charges: $1.51 billion -> $1.37 billion

Shafiq M, et al. Respiration, 2020

- 2007 – 2011 SEER-Medicare study: Only 24% of patients with rapidly recurrent, symptomatic MPE getting a definitive procedure (i.e., either IPC or pleurodesis) vs. another thoracentesis
  - associated with fewer ER visits, fewer pneumothorax episodes

Ost D, et al. Chest, 2018

- Moral: Consider definitive treatment (e.g., IPC) at first recurrence (vs. repeat thora)!

Recurrent **non-malignant** pleural effusion:

Options aplenty

- PRN thoracentesis for symptom control
- Definitive procedure (IPC, pleurodesis) for symptom control

- Steps 1, 2, and 3: Treat the underlying cause (if applicable)
  - Exudates
    - Steroids or other immunosuppressive agents
  - Transudates
    - Management of fluid overload (water/Na restriction, diuresis, etc.)
    - Optimization of dialysis regimen
    - TIPS or liver transplant

Additional considerations for managing **chylothorax**

- Low output (<1L/day)
  (e.g., 2/2 lymphoma)

- **Staged approach often appropriate:**

1. Systemic therapy (if lymphoma)
2. Dietary modifications (low-fat diet, MCT only, or NPO/TPN)
3. Somatostatin/octreotide
4. Thoracic duct ligation or embolization

- High output (>1L/day)
  (usu. post-surgical esp. esophagectomy)

- **Conservative measures likely to fail:**

- Often needs thoracic duct ligation or embolization

Itkin M, et al. J Thorac Cardiovasc Surg 2010
Paul S, et al. Thorac Cardiovasc Surg 2009

Outline

1. Working up **unexplained pleural exudates**
2. Managing **recurrent, symptomatic pleural effusions**
3. Managing **complicated pleural infections**

Management of Adults with Pleural Infection

- The Big Picture
- Antibiotic therapy
- Source control: Tube thoracostomy
- Source control: Beyond tube thoracostomy

So, you're dealing with a pleural infection. What's the Big Picture for management?

- Simple parapneumonic effusion: Antibiotics alone may work
  - Must follow up radiographically to resolution!

- Complicated parapneumonic effusion: Source control is key; tube thoracostomy imperative!
  - ~20% of cases: Need additional measures to enact complete drainage

Management of Adults with Pleural Infection

- The Big Picture
- Antibiotic therapy
- Source control: Tube thoracostomy
- Source control: Beyond tube thoracostomy

Antibiotic therapy for pleural infection

- Antibiotic choice: Often empiric if culture unrevealing (consider ID consultation)
  - Community-acquired:
    - Polymicrobial, oral flora esp. anaerobes
    - Staph aureus
    - [not always the usual CAP suspects!]
  - Hospital-acquired:
    - MDR (MRSA, GNRs)
    - Anaerobes once again
- Antibiotic duration: No robust data to guide optimal length
  - BTS 2010 guidelines recommended at least 3 weeks
  - BTS 2023 guidelines did not address this question (consider ID consultation)

Davies, H, et al. Thorax 2010
Roberts ME, et al. Thorax 2023

Management of Adults with Pleural Infection

- The Big Picture
- Antibiotic therapy
- Source control: Tube thoracostomy
- Source control: Beyond tube thoracostomy

Achieving source control: Tube thoracostomy best practices

- Size doesn't matter
  - (or does it?)
  - No RCTs, but data [and BTS 2023 guidelines] suggest ≤14Fr (e.g., pigtails)
- Flushing matters
  - (or maybe not?)
  - Oft-quoted best practice: 10-30cc saline q6-8h
- Suction matters
  - (or maybe not?)
  - Common practice: -20 or -10 cm H2O

Roberts ME, et al. Thorax 2023

Management of Adults with Pleural Infection

- The Big Picture
- Antibiotic therapy
- Source control: Tube thoracostomy
- Source control: Beyond tube thoracostomy

Achieving source control: When tube thoracostomy is not enough

- TPA/DNase
  - via chest tube
- Thoracic surgery

More about TPA/DNase

- The What:
  - Intrapleural 5mg DNase + 10mg TPA BID x 3 days
  - Dwell time of each administration (4/day): 1 hour
  - CT chest @ baseline and post-treatment
- The Why:
  - MIST-2 RCT:
    - ↓ surgical referral for unresolved infection at 3mo (4% vs. 16%)
    - Decreased LOS (−6.7 days [95% CI −12.0 to −1.9]; p = 0.006)
    - 6% serious but nonfatal AEs (hemothorax, hemoptysis)

Rahman N, et al. NEJM 2011

How to administer TPA/DNase (or flush saline) through a pigtail chest tube

Side port with a clamp
(Arrow® Percutaneous Cavity Drainage Catheter)

Side port connected to 3-way stop-cock
(Cook® Wayne Pneumothorax Catheter)

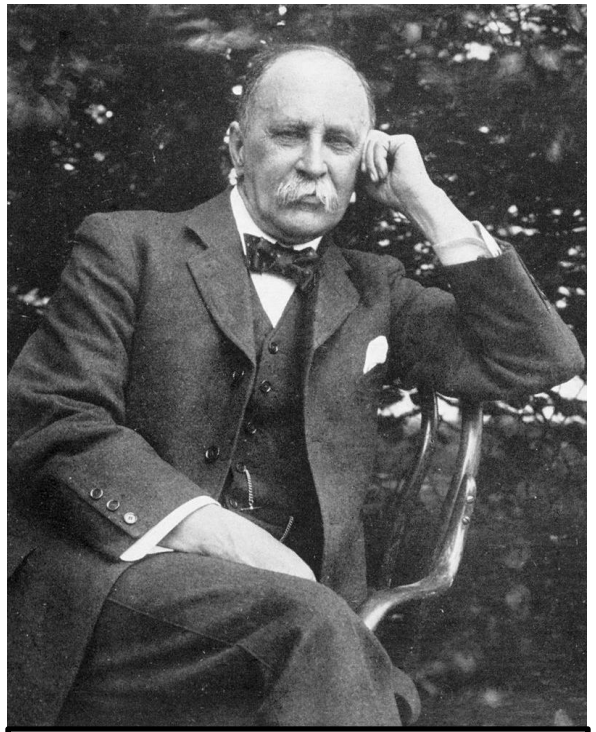
Thoracic surgery for source control

- Commonly VATS or RATS, sometimes open thoracotomy
  - Debridement/washout (uncommonly via medical pleuroscopy)
    - Debridement and evacuation of infected material
  - Decortication
    - If visceral pleura developed a thickened rind
    - In order to allow adequate lung re-expansion

What's the best way to treat unresolving pleural infection: A trial of TPA/DNase or early thoracic surgery?

- An age-old question!

- Sir William Osler (1849 – 1919)
  - Died during the Spanish flu pandemic from a superadded pleural infection
  - Autopsy report:
    - "unresolved pneumonia,
    - multiple lung abscesses and
    - an empyema"

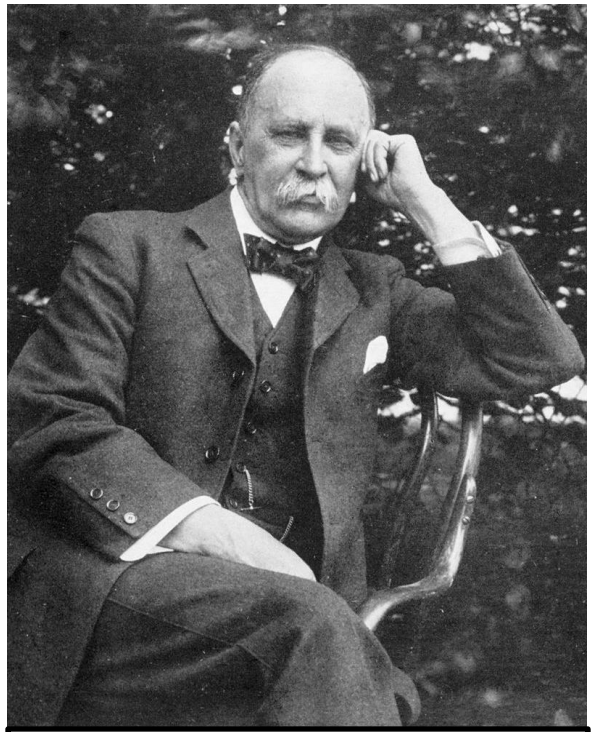


Credit: Osler Library of the History of Medicine, McGill University.

Osler preferred surgery to medicine for treatment of unresolving pleural infection

- *"Empyema needs three inches of cold steel instead of the fool of a physician"*

- Caveats
  1. There were no antibiotics in his era
  2. He did not get a chest tube
     - Let alone TPA/DNase
  3. He died from massive post-op hemorrhage
     - (Following open surgical drainage)
     - But, there was no VATS or RATS in his era either!



Credit: Osler Library of the History of Medicine, McGill University.

What's better for unresolving pleural infection: A trial of TPA/DNase or early thoracic surgery?

- Nearly equivalent cost-effectiveness
- Cochrane review of limited data: Early VATS may reduce LOS

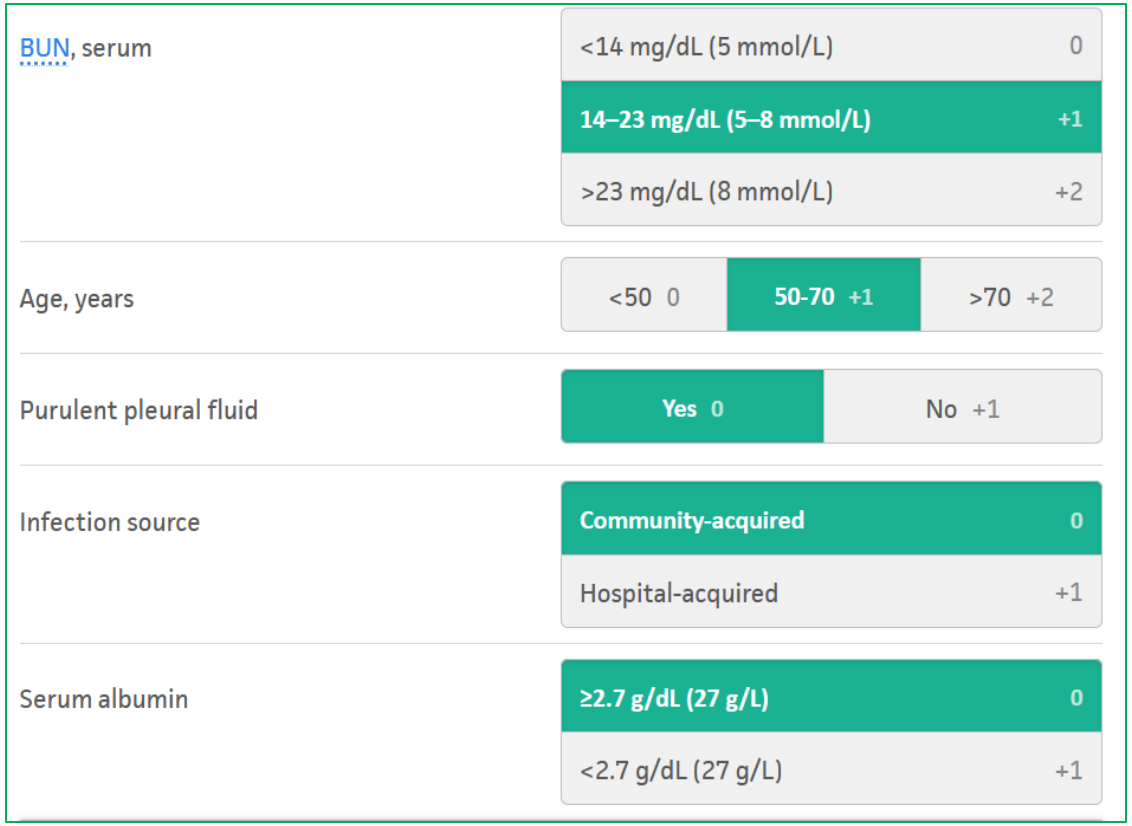
- One possible approach:
  - Consult thoracic surgery early if pleural infection suspected; don't take too much comfort in (-) fluid G stain & culture as it may forever be (-)!
    - Late referral associated with higher conversion to thoracotomy
    - ?VATS upfront for worse prognosis (if surgical candidate)

Shipe et al. Ann Thor Surg 2020
Cochrane Review 2017. https://doi.org/10.1002/14651858.CD010651.pub2

Prognosticating pleural infection patients: The RAPID score

- Prospective validation study (PILOT):
  - RAPID score predicts 3-month mortality

- Low-risk (1-2): 2.3%
- Medium (3-4): 9.2%
- High-risk (5+): 29.3%



Rahman NM, et al. Chest. 2014
Corcoran JP, et al. ERJ 2020