Pleural Diseases
Pleural Effusions & Pneumothorax

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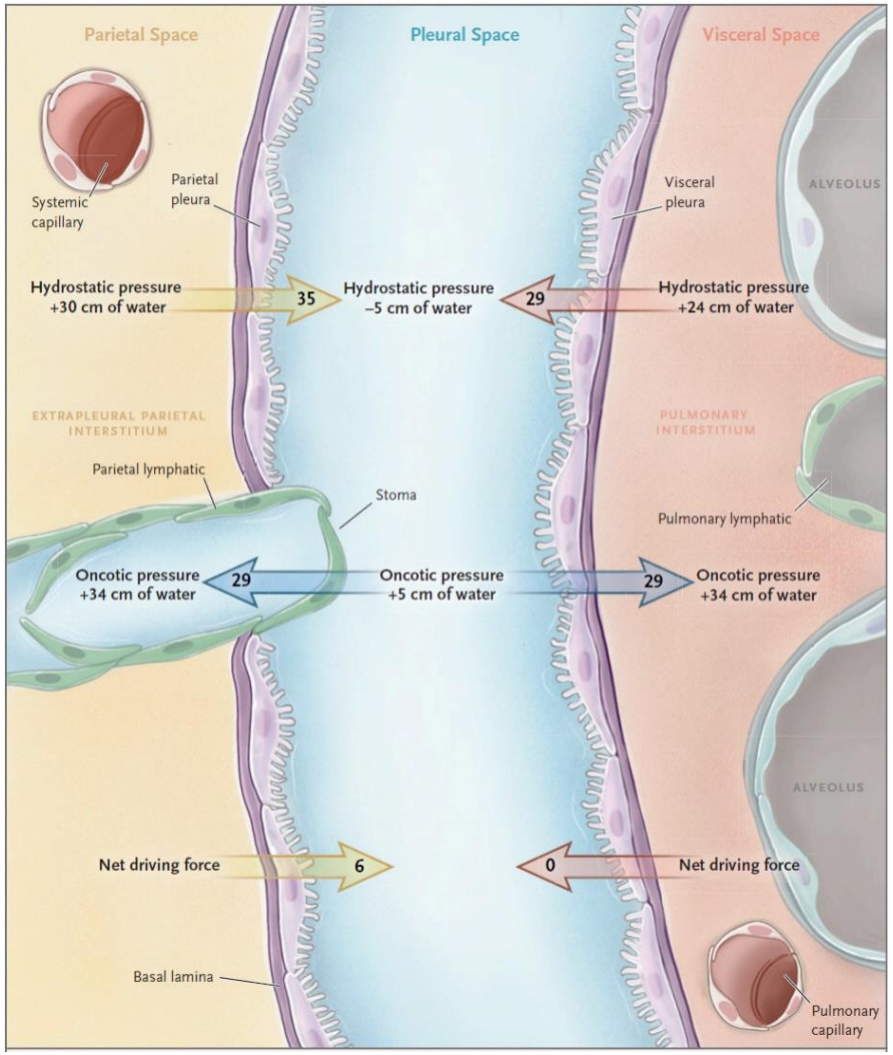
Outline

- Pleural anatomy and physiology
- Pleural effusions
  - Transudate vs exudate
  - Common types of pleural effusions
  - Parapneumonic effusions and pleural infections
    - Pleural TB
  - Malignant pleural effusions
- Pneumothorax

Pleural Effusions

Pleural Structure and Physiology

- Fluid is both produced and absorbed on the parietal surface
- Balance of hydrostatic and oncotic pressure
- 8-10 mL (0.26 mL/kg) in each pleural cavity

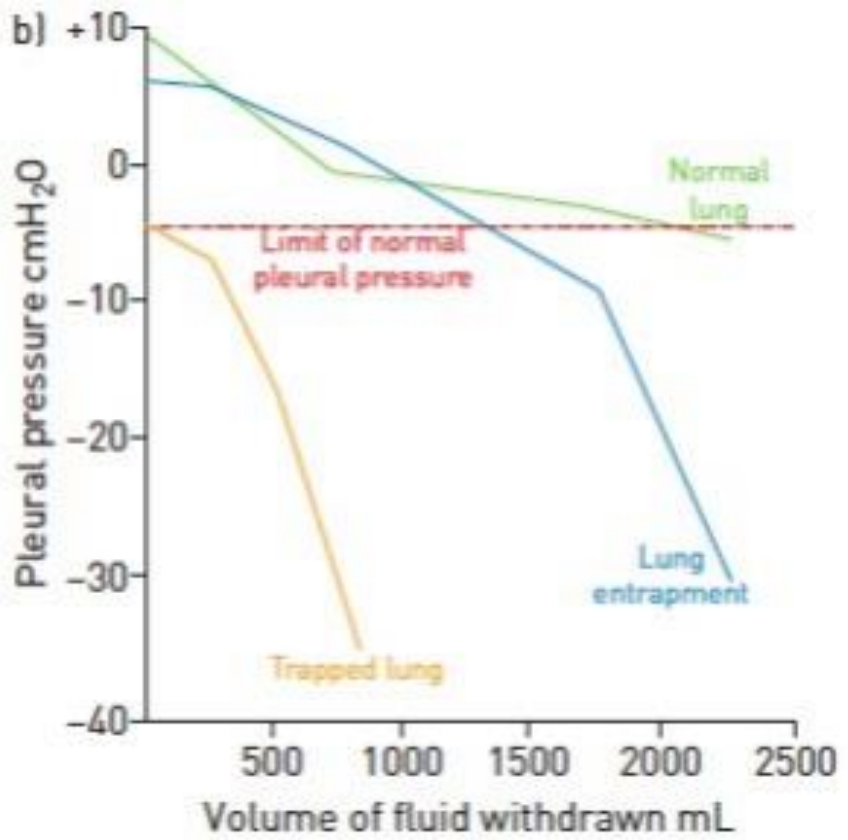


Pleural physiology

- Pleural pressure -3 to -5 cm H2O
- Lung elastic recoil inward
- Chest pulls outward

Pleural elastance

- Change in pleural pressure/volume removed
- “Normal” is 0.5 to <14.5 H2O/L
- Trapped lung elastance will be high



Pleural Effusions
Clinical symptoms and signs

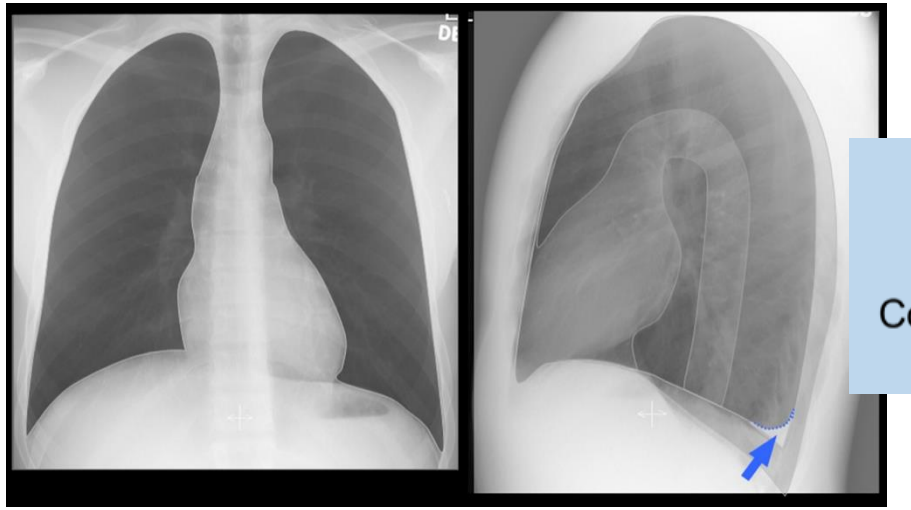
Symptoms:

- Dyspnea
- Inability to take a deep breath
- Sensation of fullness or pressure
- Pleuritic pain is usually a sign of infection or malignancy (parietal pleural)

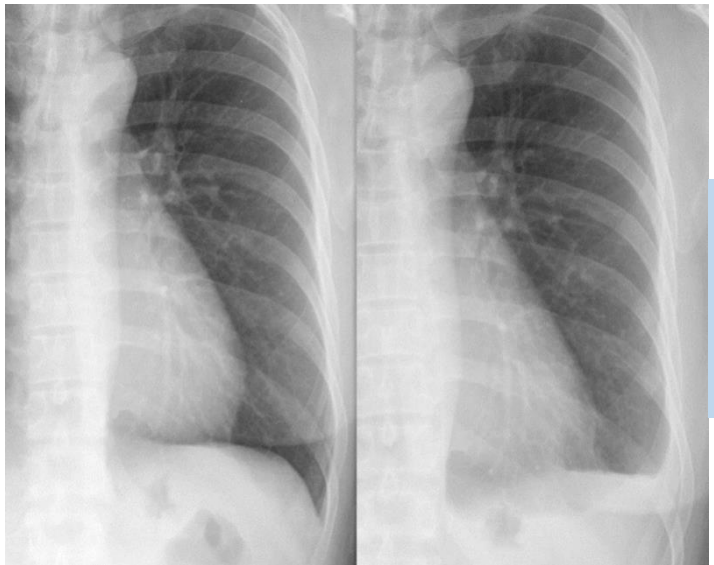
On Exam:

- Diminished breath sounds
- Increased tactile fremitus
- Dullness to percussion/Loss of tympanicity

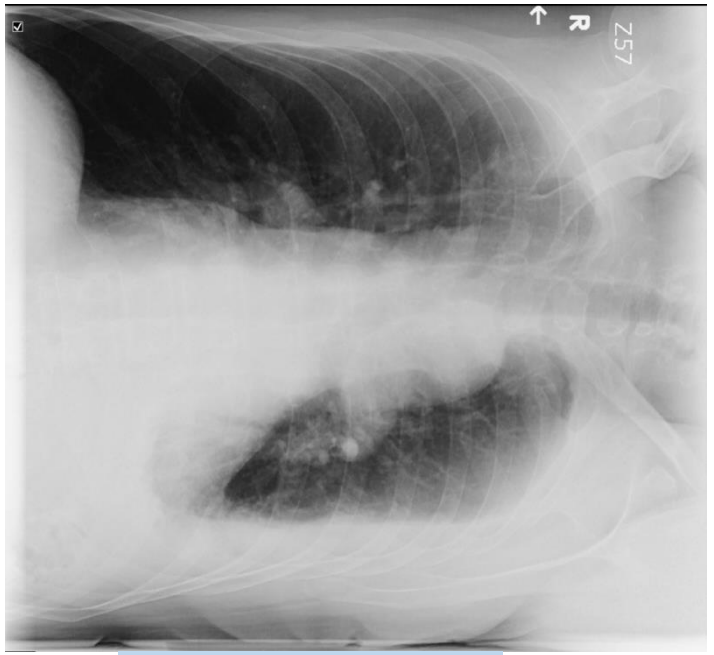
Pleural Effusions Diagnosis: Xray



50 cc
Lateral View
Posterior
Costophrenic Angle
Blunting

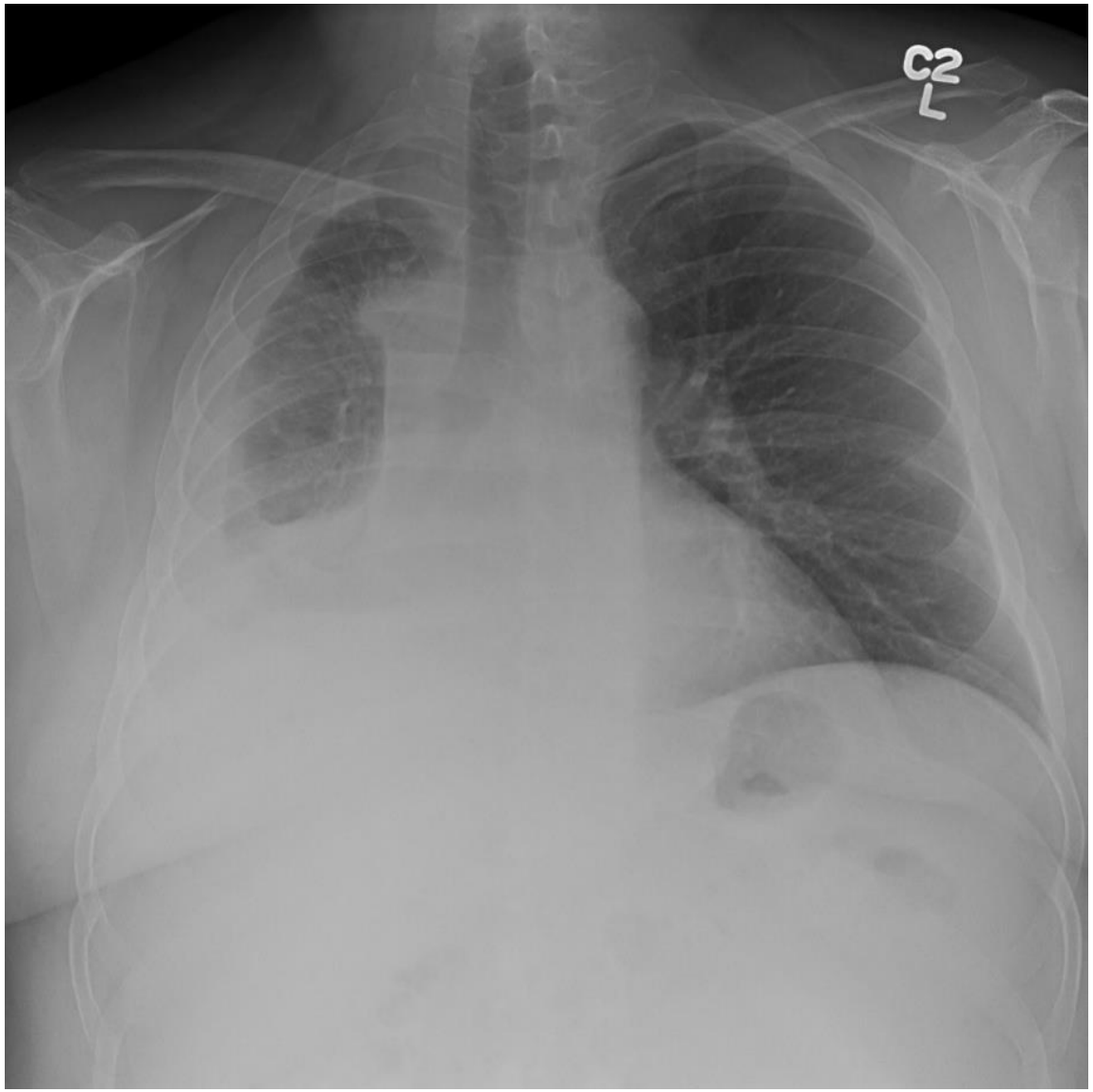


175-200 cc
Frontal View
Lateral costophrenic
angle blunting



200 cc
Lateral Decubitus
1 cm thick

Ipsilateral shift = volume loss due to an associated atelectasis

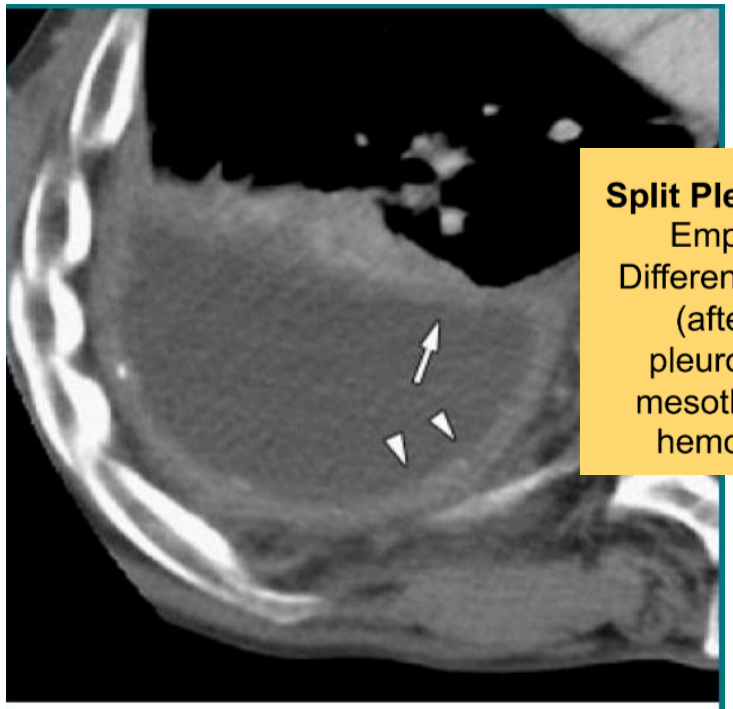


Pleural Effusion Diagnosis
CT

- With contrast better
- Clear delineation between lung & pleural tissue

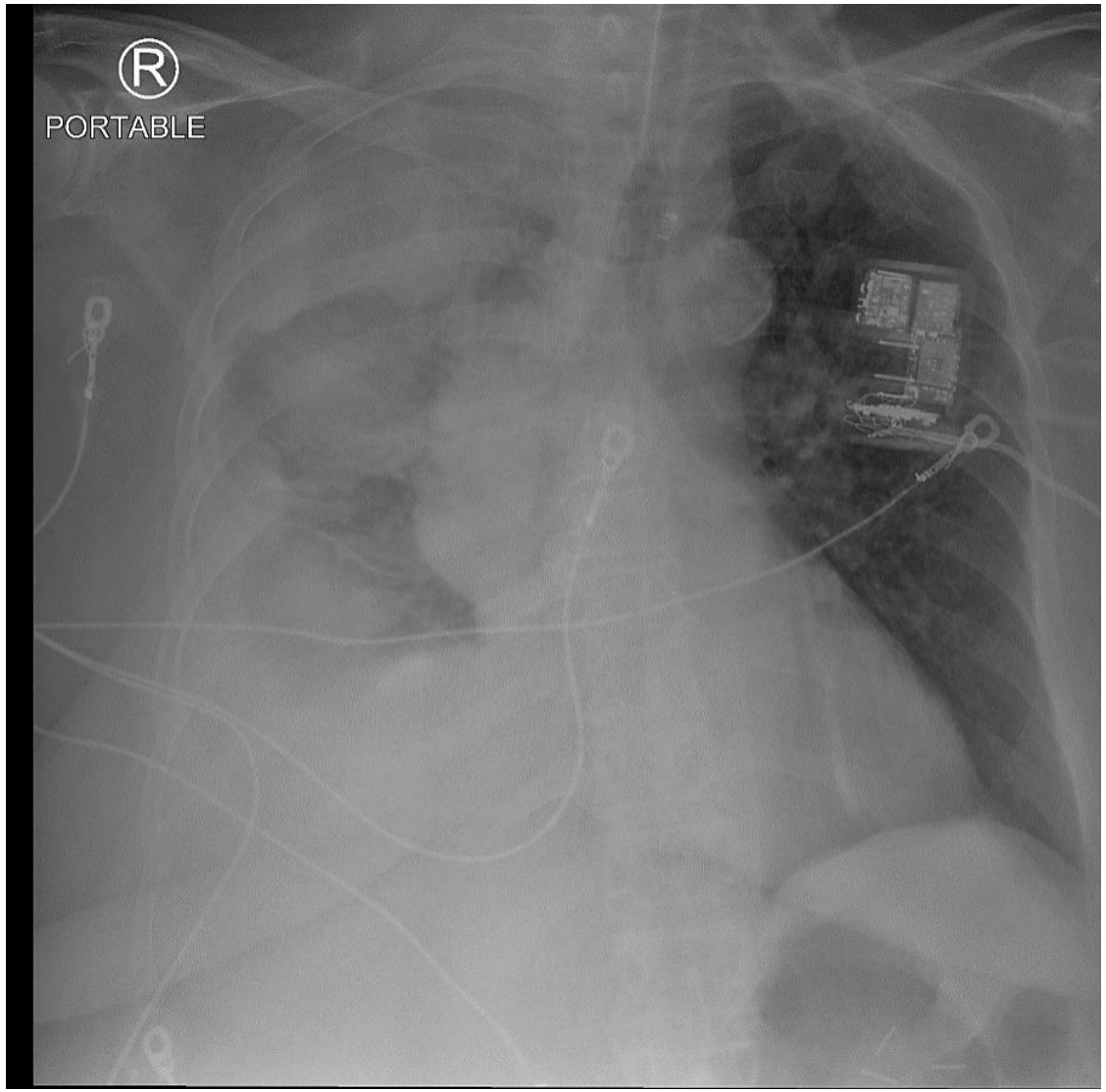
  - Lung mass Vs loculated effusion

  - Pleural fluid Vs pleural thickening



Split Pleural Sign
Empyema
Differential: MPE (after talc pleurodesis), mesothelioma, hemothorax

Contrast-enhanced transverse CT scan shows empyema between thickened parietal (arrowheads) and visceral (arrow) pleural layers: the split pleura sign.

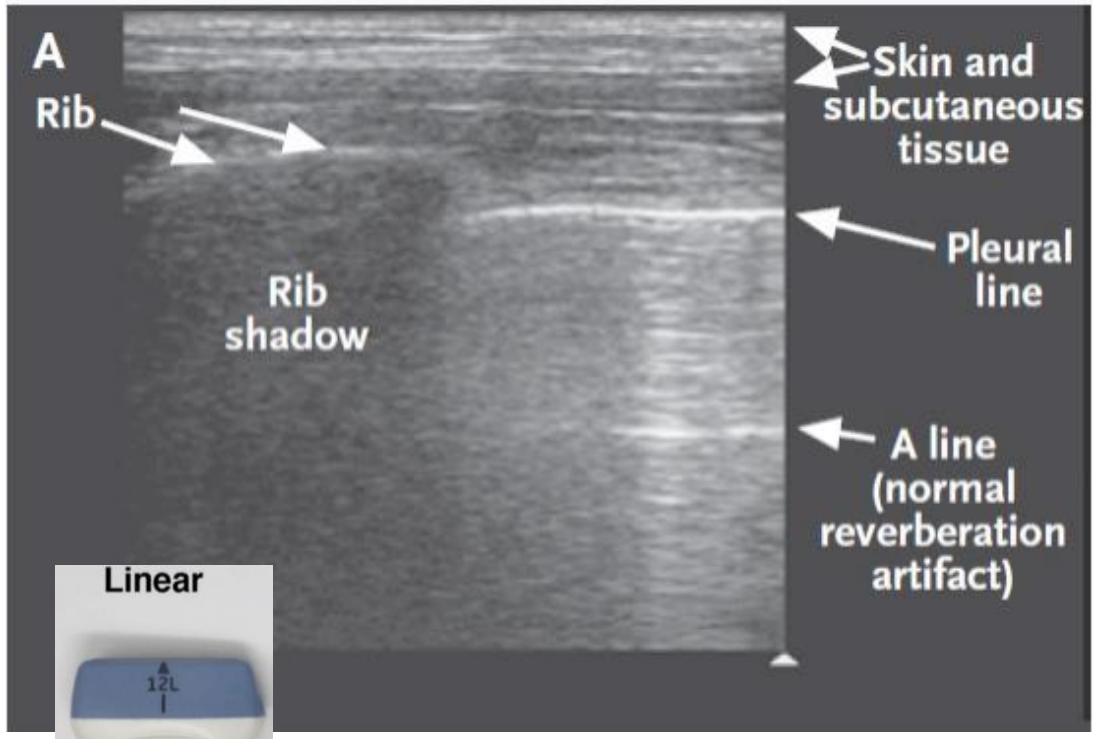




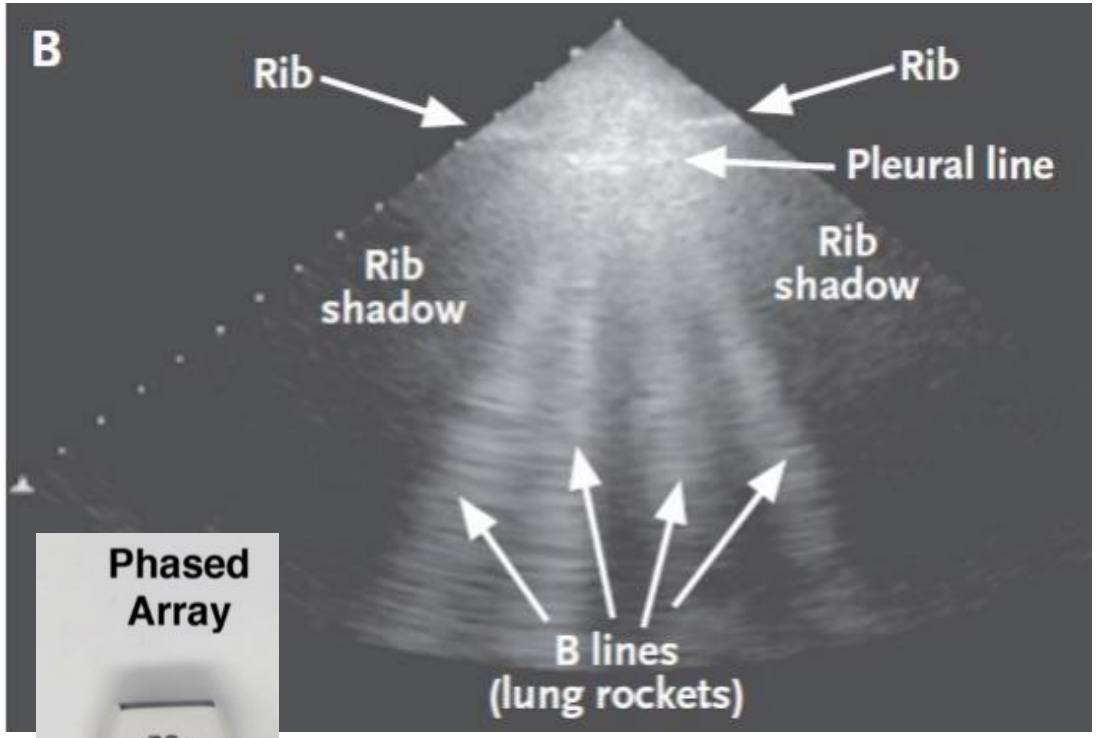
Loculated pleural effusion:

Infection
Malignancy
Simple effusion with pleural adhesions due to prior trauma, surgery

Pleural Effusion Diagnosis Ultrasound



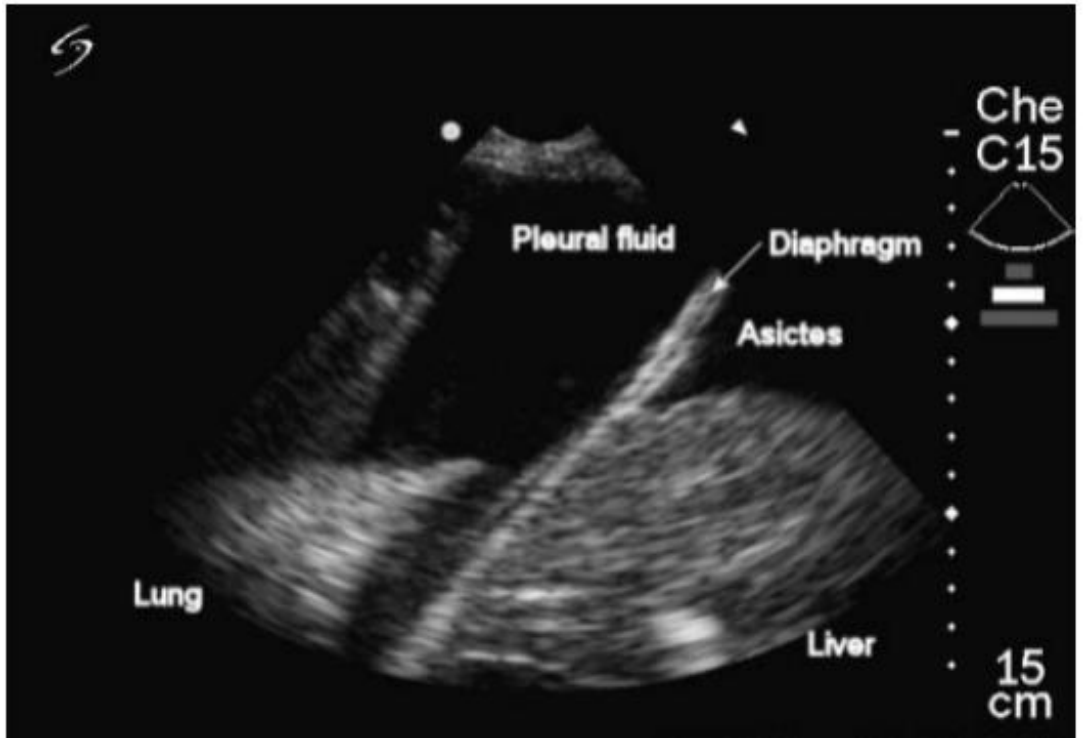
A lines = normal finding in healthy, aerated lungs and represent reverberation artifacts



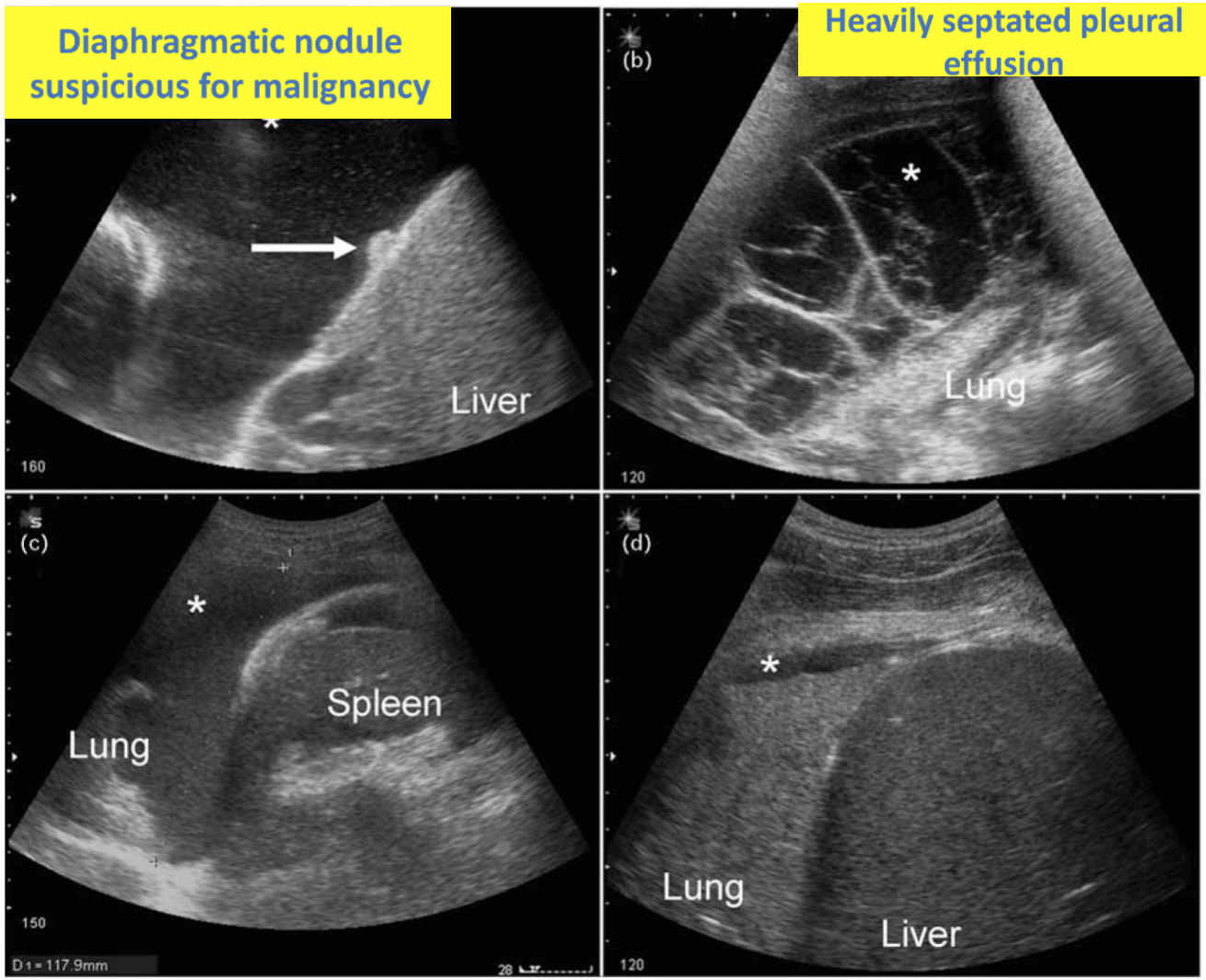
B lines = reverberation artifacts due to thickening of the interlobular septa, often indicating interstitial fluid or edema

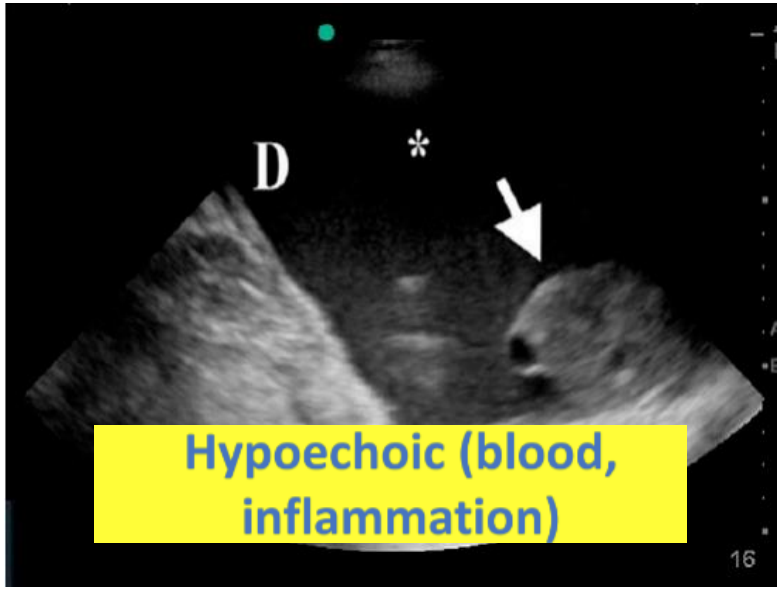
Pleural Effusion Diagnosis Ultrasound

- Standard of care for all pleural procedures
- Reduced risk of pneumothorax
  - from 10-18% to 3-4%



Pleural Effusion Diagnosis: Ultrasound



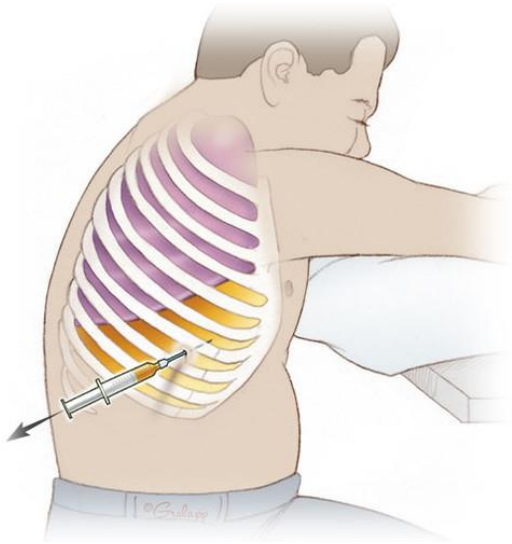


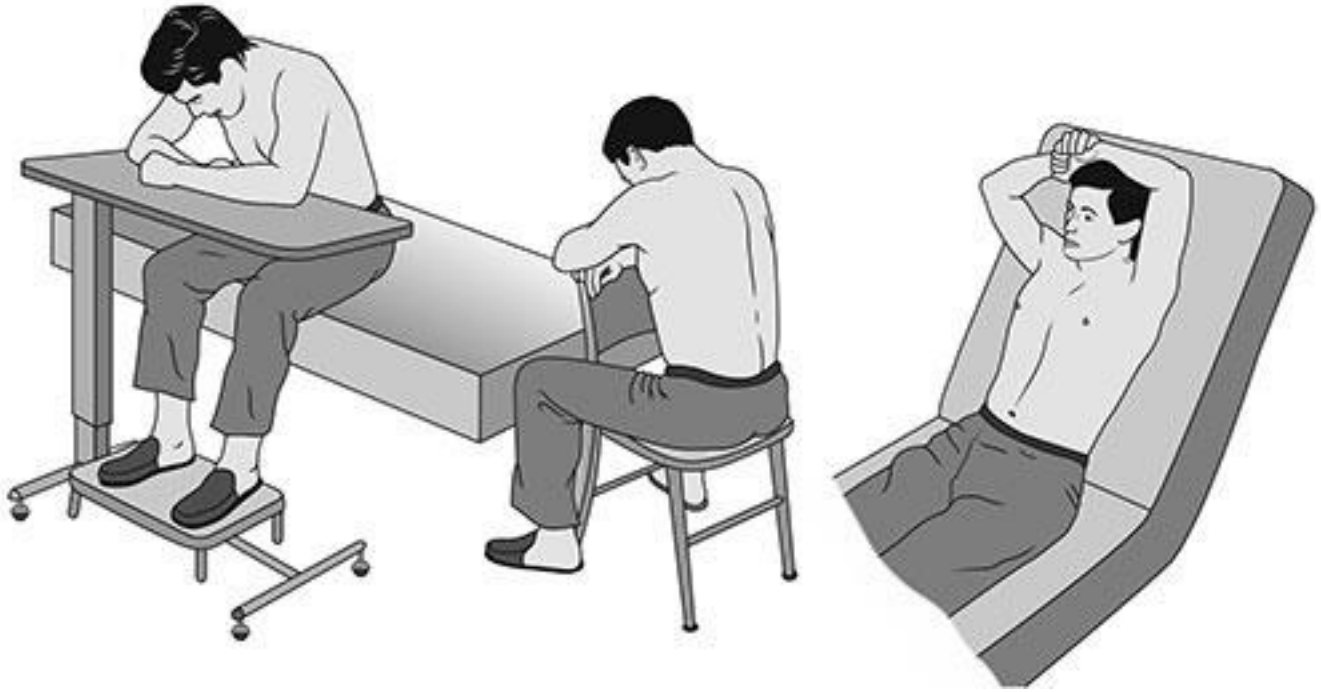
Pleural effusions
General approach and management

- Full H&P and Exam:
  - CHF, Cirrhosis, renal failure, trauma, pneumonia, cancer, PE
  - Pleuritic pain indicates inflammatory process
- Imaging studies: X ray, US and CT
- Does it need diagnostic or therapeutic drainage?
  - Size
  - Acuity and severity of symptoms
  - Known or suspected etiology
  - Recurrent vs new
- If drainage is decided, test pleural fluid:
  - Light's Criteria
  - Chemistries, cell count diff, cultures, cytology

Thoracentesis

- Diagnostic
- Therapeutic





Thoracentesis Contraindications

Absolute Contraindications:

- Chest wall cellulitis at the site of puncture
- Uncorrected coagulopathy or thrombocytopenia *
- Lack of patient cooperation or consent

Relative contraindications:

- Bullous disease
- Positive end-expiratory pressure/mechanical ventilation
- Only one functioning lung
- Small volume of fluid (<1 cm thickness on a lateral decubitus film)

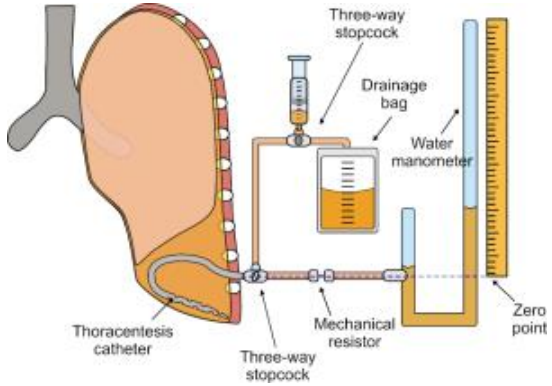
Thoracentesis
When do you stop drainage?

Symptom Limited

- chest pain 2/10, persistent cough or dyspnea

Manometry

- Reflects pleural space elastance
- Identifies trapped and entrapped lung
- May help predict re-expansion pulmonary edema but not superior to symptom-limited approach



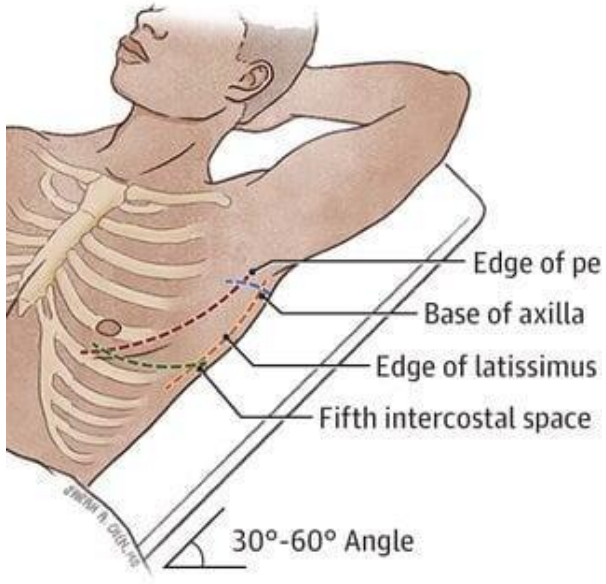


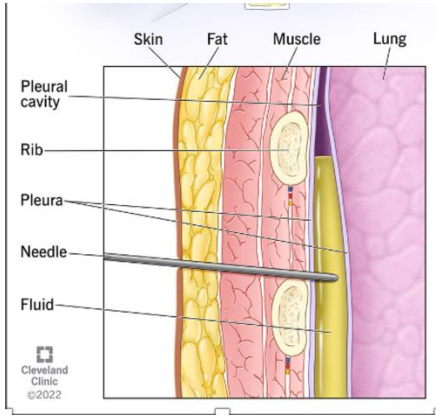
Thoracentesis Complications

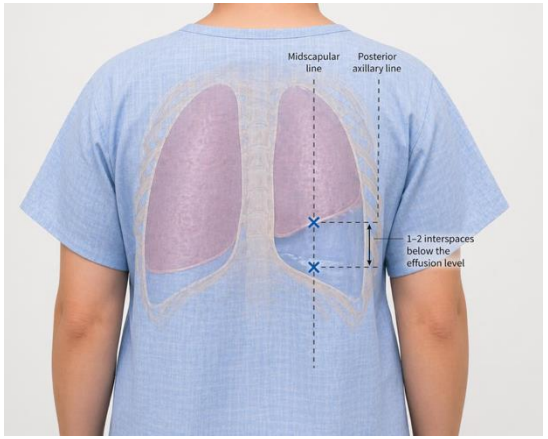
- **Pneumothorax**
  - Risk factors: low BMI (<18 kg/m²), large volume extraction, multi-pass attempts, and absence of real-time ultrasound.
  - Prevention: use real time US
- **Hemothorax**
  - Risk factors: elderly patients
  - Prevention: lateral location, safety triangle, upper rib border
- **Re-expansion pulmonary edema**
  - Risk factors: large-volume drainage (>1.5 L) + low lung elastance
  - Avoid rapid large volume removal, stop when pain is reported
- **Splenic or liver laceration**
  - Prevention: real time US
- **Soft tissue/pleural space infection**
  - Use sterile technique

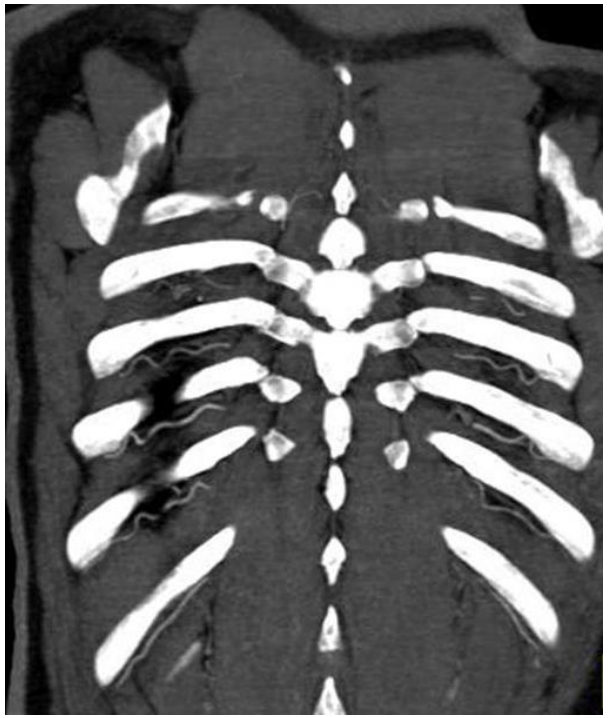
Hemothorax complication of thoracentesis

- Intercostal artery injury or pleural tumor bleeding
- Pain, tachycardia, post procedure Xray with no resolution of effusion or worsening effusion
- Triangle of safety:
- Stay close to upper rib border



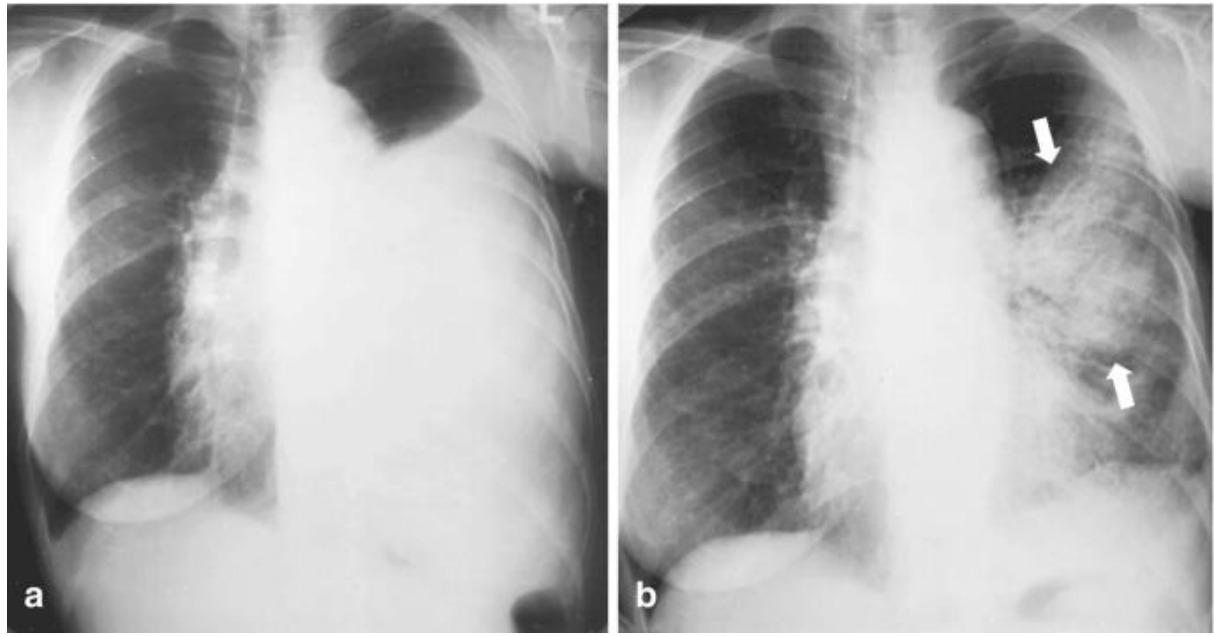






Re-expansion pulmonary edema

- Rare, but potentially fatal
- Correlates to lung elastance >> volume removed
- Supportive care: Oxygen, Positive Pressure (BiPAP, Mechanical Ventilation)



Pleural Effusion Diagnosis
Pleural Fluid Analysis

Light criteria: (exudative vs transudative)

- Pleural fluid/serum protein >0.5
- Pleural fluid/serum LDH >0.6
- Pleural fluid LDH > two-thirds of upper normal limit for serum

Modified Light criteria (no serum values):

- Pleural fluid protein > 3.0 g/dL
- Pleural fluid cholesterol > 55 mg/dL
- Pleural fluid LDH > 0.45 x upper limit of normal serum LDH

Additional Studies

- Gross Appearance
- Cell Count & Differential
- Gram Stain, C & S
- Cytology
- Glucose
- Cholesterol
- Amylase
- PH

Pleural Fluid Analysis Appearance

Description	Possible Etiology
Black	Aspergillus niger
Milky	Chylothorax
Yellow-green	Rheumatoid pleuritis
Pus	Empyema
Anchovy paste	Amebic liver abscess

Description	Etiology
Bloody	Hemothorax, Cancer, PE, Trauma
Ammonia odor	Urinothorax
Brown	Old blood, Amebic liver abscess
Green	Bilopleural fistula
Water-like	Duro-pleural fistula



Pleural Fluid Analysis Chemistries

Chemistry	Etiologies
LDH > 1000	Empyema, complicated parapneumonic effusion, cholesterol effusion, rheumatoid pleurisy, primary pleural lymphoma, paragonimiasis
Low glucose	Empyema, chronic rheumatic pleurisy, esophageal rupture, malignancy, paragonimiasis, acute lupus pleuritis, tuberculosis
High amylase	Acute pancreatitis, esophageal rupture, malignancy
Total protein > 7 to 8 g/DL	Multiple myeloma, rheumatoid pleurisy, Waldenstrom's macroglobulinemia

Total protein < 1 g/DL
Duropleural fistula
Urinothorax
Peritoneal dialysis

Pleural Fluid Analysis
Cell Count Predominance

Predominant cell	Etiologies	With low pH < 7.30
Lymphocytosis	Malignancy, lymphoma, chronic rheumatoid pleurisy, chylothorax, Post-CABG, sarcoidosis, tuberculosis, uremic effusion, yellow nail syndrome	Malignancy, chronic rheumatic pleurisy, tuberculosis
Eosinophilia (>10%)	Pneumothorax (within hours), hemothorax (after 10 to 14 days), pulmonary infarction, parasitic or fungal disease, drug induced, lymphoma, carcinoma (8%)	Paragonimiasis
Neutrophilia	Acute pleural injury, infection, inflammation	Empyema, acute esophageal rupture, acute lupus pleurisy, cholesterol effusion

Pleural Fluid Analysis
PH

- Collect fluid anaerobically in heparinized syringe, place on ice immediately, remove residual lidocaine, analyzed in blood gas analyzer within 1 hour
- Air & time in the syringe increases pH; lidocaine decreases pH
- Pleural fluid glucose is alternative to pH; not affected by air, heparin, lidocaine

Pleural Fluid Acidosis (pH < 7.3)

Empyema
Esophageal rupture
Chronic rheumatoid pleurisy
Cholesterol effusion
Malignancy
Tuberculosis
Acute lupus pleuritis
Paragonomiasis

Pleural Effusion Classification
Transudative Effusions

Transudate

Develops when low-protein fluid leaks across an intact capillary barrier because of increased hydrostatic pressure or decreased osmotic pressure

Transudative effusions

- Congestive heart failure
- Cirrhosis
- Nephrotic syndrome
- Glomerulonephritis
- Peritoneal dialysis
- Hypoalbuminemia (typical serum albumin, <1.5 mg/dl)
- Atelectasis
- Superior vena cava obstruction
- Trapped lung
- Sarcoidosis
- Myxedema
- Cerebrospinal fluid leak or ventriculopleural shunt
- Urinothorax
- Pulmonary arterial hypertension
- Pulmonary embolism
- Pericardial disease
- Extravascular migration of central venous catheter

*25-30% of transudates can be misclassified using Light's criteria as exudates – CHF on diuretics

Heart Failure-Related Pleural Effusions

Mechanisms:

- Increased PCWP (LV filling pressures) and/or CVP (RV)
- Reduced lymphatic clearance

Laterality:

- Typically **bilateral (70–75%)**.
- When unilateral, more frequently on the **right side**

Characteristics:

- **Transudate**
- Up to **30% pseudo-exudates** due to hemoconcentration of pleural proteins
  - Serum-to-pleural fluid **albumin gradient >1.2 g/dL** or **protein gradient >3.1 g/dL** confirms a transudative cardiac etiology

Renal disease-related transudative effusions

Nephrotic Syndrome

CXR bilateral effusions
Albumin < 2.0

*PE may occur in 20% acquired Protein S Deficiency

Treat nephropathy and avoid serial thoracentesis



Transudates

Urinothorax

Rare complication of obstructive uropathy

Creatinine
Pleural fluid > serum
Low pH and glucose

Renal Scintigraphy – tracer flow from urinary tract to pleural space

Peritoneal Dialysis

Fluid moves thru defects in diaphragm
Most within 30 days of PD, but can occur > 1 year
CXR with right sided effusion
PF Glucose levels very high

Treatment
-Stop PD for 2 to 6 weeks, 50% can resume
-Consider pleurodesis of VATS

Glycinothorax
Bladder irrigation using glycine solutions
Perforation of the bladder spills glycine solutions

Hepatic Hydrothorax

- Liver cirrhosis & portal hypertension
- 80 % right-sided
- May not be associated with ascites
- Peritoneal to pleural: diaphragmatic micro-fenestrations & pressure gradient (vacuum effect)
  - Hypoalbuminemia, lymphatic overload as other mechanisms

- Treatment
  - Same medical management as ascites
  - Sodium restriction & lowering portal pressures
  - TIPS (transjugular Intrahepatic portosystemic shunt) in refractory cases
  - Liver transplant
  - Avoid repeated interventions or chest tube due to protein loss and renal failure

- Complications
  - Spontaneous infection of hydrothorax (15%)
    - PF neutrophil count > 250 cells/uL with +culture or > 500 cells/uL with -cx

Pleural Effusion Classification
Exudative Effusions

Exudate

Develops when fluid leaks across an altered capillary barrier with increased permeability, thus allowing transfer of protein and liquid

Represents an inflammatory process of the lung or pleura

Exudative effusions

Infectious: bacterial, viral, tuberculosis-related, fungal, parasitic

Neoplastic: metastatic disease (e.g., lung cancer, breast cancer, lymphoma, myeloma, ovarian cancer, pancreatic cancer, cholangiocarcinoma), mesothelioma, primary body-cavity lymphoma

Paramalignant effusions: reactive pleuritis due to underlying lung cancer, airway obstruction or atelectasis, radiation-induced pleuritis

Reactive: reactive pleuritis due to underlying pneumonia (i.e., parapneumonic)

Embolic disease: pulmonary embolism

Abdominal disease: pancreatitis, cholecystitis, hepatic or splenic abscess, esophageal perforation after esophageal varix sclerotherapy

Cardiac or pericardial injury, including myocardial infarction (after coronary-artery bypass, cardiac surgery, or cardiac ablation procedures), pulmonary-vein stenosis

Gynecologic: ovarian hyperstimulation, Meigs' syndrome, endometriosis, postpartum complications

Collagen vascular disease: rheumatoid arthritis, systemic lupus erythematosus, Sjögren's syndrome, familial Mediterranean fever, eosinophilic granulomatosis, granulomatosis with polyangiitis

Medications: nitrofurantoin, dantrolene, methysergide, dasatinib, amiodarone, interleukin-2, procarbazine, methotrexate, clozapine, phenytoin, β-blockers, ergot drugs

Hemothorax

Chylothorax (most commonly seen after trauma or in patients with lymphoma)

Sarcoidosis

Lymphoplasmacytic lymphoma

Cholesterol effusions (commonly seen in tuberculosis, rheumatoid effusions, and any other chronic pleural effusion)

Miscellaneous: benign asbestos pleural effusion, yellow nail syndrome, uremia, drowning, amyloidosis, electrical burns, iatrogenic effusion, capillary leak syndromes, extramedullary hematopoiesis

Common Exudative Pleural Effusions

Effusions after Cardiac Surgery

Characteristic	Post-CABG	PCIS
Clinical	Dyspnea	Fever, pleuritic chest pain, pericardial rub
Pathogenesis	Early: due to surgical trauma Late: unknown	Myocardial or pericardial injury
Imaging	Mostly small unilateral left-sided, 10% large	Small effusion, unilateral or bilateral Parenchymal infiltrate
Appearance	Early: Bloody Late: Clear Yellow	Bloody or serosanguinous
Cell count differential	Early: neutrophilic or eosinophilic Late: lymphocytic	PMNs or mononuclear cells
pH and glucose	Normal	Normal
Anti-myocardial antibody	Absent	High titer
Treatment	Serial thoracentesis	NSAIDS or corticosteroids Colchicine effective in prevention

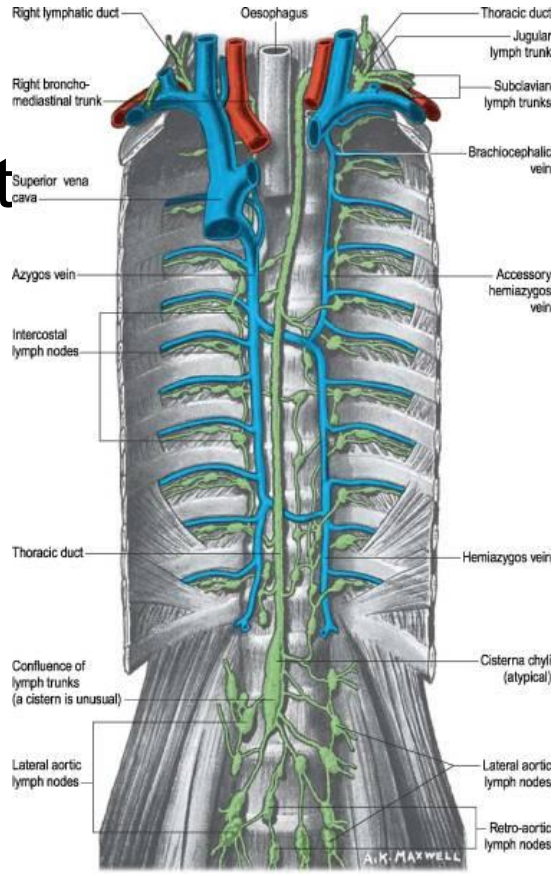
Post-Cardiac Injury Syndrome (PCIS)

Can occur after myocardial infarction, after cardiac surgery or after trauma

Chylothorax

Traumatic

- at level of T5, thoracic duct crosses from right to left
  - Below level of crossing: right-sided;
  - Above: left-sided
- Post-surgical



Non-traumatic

- Malignancy: Lymphoid, Lung
- Yellow Nail Syndrome:
  - deformed yellow nails, lymphedema, effusion
- Lymphangioleiomyomatosis:
  - females, cystic lung disease, mutations in tuberous sclerosis complex-2 gene, angiomyolipomas

Chylothorax Diagnosis

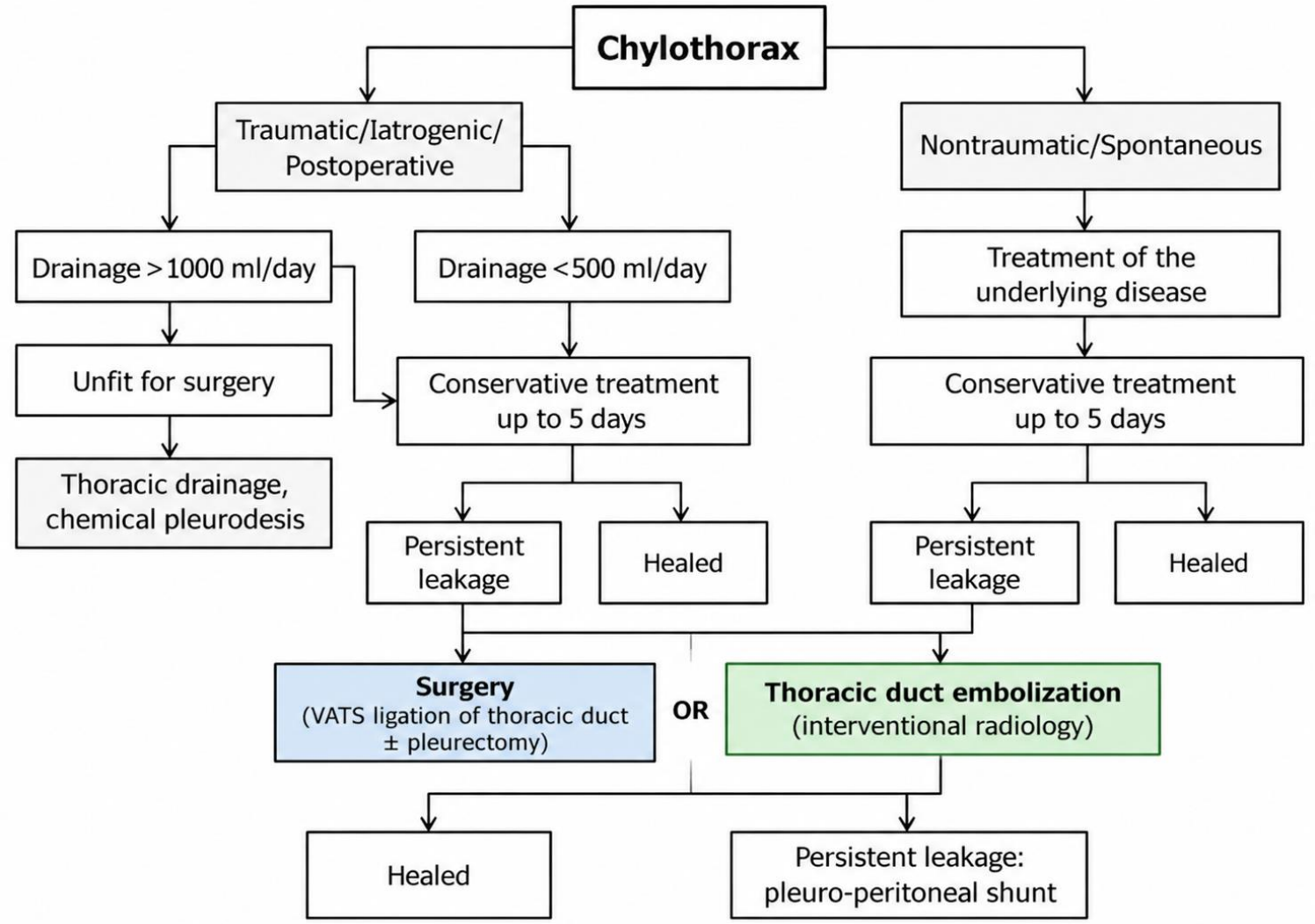
Triglycerides > 110
Send chylomicrons
Turbid, milky
Chyle in pleural space from thoracic duct obstruction

Pseudochylothorax
Cholesterol > 220 mg/dL
No chylomicrons
Tuberculosis or Rheumatoid
Observation





Chylothorax Management



Conservative management of chylothorax:

- Low-fat, high-protein diet with medium chain triglycerides
- +/- NPO and TPN
- Drainage: frequent thoracentesis or chest tube
- Octreotide: 50-100 mcg sq q8h

Ur Rehman K, Sivakumar P. Non-traumatic chylothorax: diagnostic a nd therapeutic strategies. Breathe. 2022;18(2):210163

RA and SLE-pleural effusions

Rheumatoid Arthritis-Pleural Effusion

- 20% on autopsy, 5% clinically
- Males>females, seropositive, long-standing RA
- +/- rheumatoid nodules
- Usually unilateral, small to moderate size, more common on left side
- Typically, pH< 7.20; glucose <50mg/dL; pleural/serum glucose ratio <0.5; elevated LDH (>1,000 U/L), rheumatoid titer > 1:320

Systemic Lupus Erythematosus-Pleural effusion

- 30%
- Pleurisy +/- effusions: most common thoracic manifestation
- Usually small, bilateral, exudate
- PF ANA (titer >1:160, PF/S > 1) supports diagnosis but not diagnostic by itself
- Low C3, C4 helpful but not specific
- Presence of LE cells is highly specific, but rarely used clinically

Pleural effusions
Treatment principles

Transudates:

- Widely variable depending on etiology
- Observe if small
- Diuresis (CHF, cirrhosis, nephrotic syndrome)
- Drainage (if moderate-large)
- Treat underlying cause

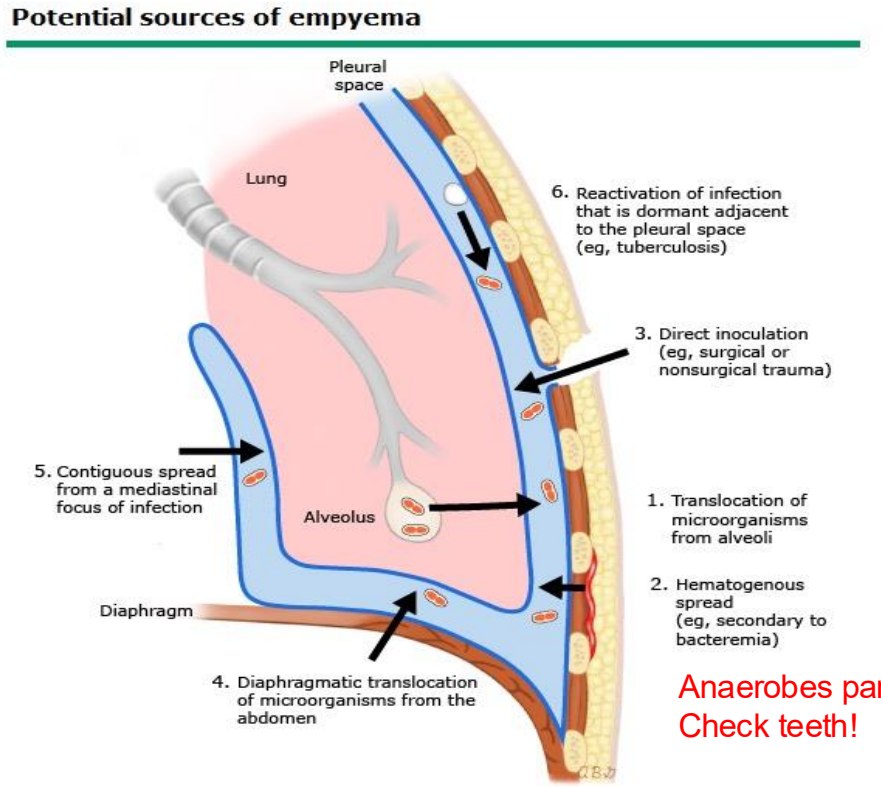
Exudates:

- Widely variable depending on etiology
- Observe if small
- Drainage more common
- Diuresis often unsuccessful
- Treat underlying cause

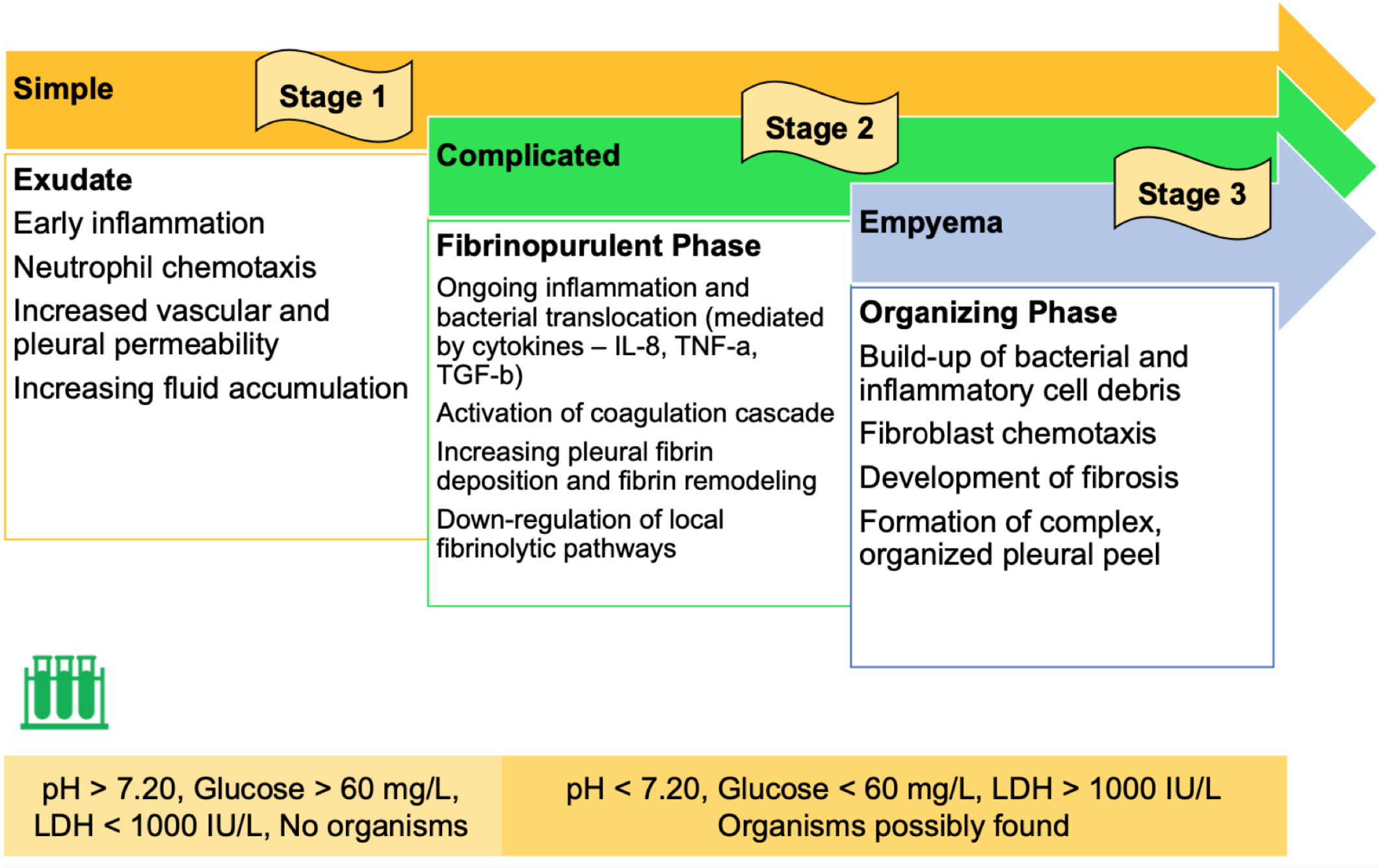
Parapneumonic Effusions and Pleural Space Infections

Parapneumonic effusions

- Pleural effusions adjacent to bacterial pneumonia
- 20 to 57% of pneumonias
- Increasing incidence
- 25% prolonged hospitalization (>1 month)
- 10-20% mortality
- Male predominant (68%)
- Most <65 years old



Anaerobes particularly common
Check teeth!


Simple
Stage 1
Exudate
Early inflammation
Neutrophil chemotaxis
Increased vascular and pleural permeability
Increasing fluid accumulation
Complicated
Stage 2
Fibrinopurulent Phase
Ongoing inflammation and bacterial translocation (mediated by cytokines – IL-8, TNF-a, TGF-b)
Activation of coagulation cascade
Increasing pleural fibrin deposition and fibrin remodeling
Down-regulation of local fibrinolytic pathways
Empyema
Stage 3
Organizing Phase
Build-up of bacterial and inflammatory cell debris
Fibroblast chemotaxis
Development of fibrosis
Formation of complex, organized pleural peel
pH > 7.20, Glucose > 60 mg/L, LDH < 1000 IU/L, No organisms
pH < 7.20, Glucose < 60 mg/L, LDH > 1000 IU/L
Organisms possibly found

Bacteriology (US/Europe)

COMMUNITY ACQUIRED 85%		
AEROBES 73%	*STREPTOCOCCI* 72%	*Strep. milleri group* 46%
		Strep. pneumoniae 40%
		Strep. pyogenes 5%
		Other streptococci. 9%
	STAPHYLOCOCCI 14%	*S. aureus* 77%
		MRSA 20%
		S. epidermidis 3%
	GRAM NEGATIVE 12%	
	OTHER 2%	
ANAEROBES 22%	**'Anaerobes'** includes Fusobacterium, Bacteroides, Peptostreptococcus , Unclassified mixed anaerobes, *Prevotella* spp., *Clostridium* spp., *Mycobacterium tuberculosis* and *Actinomyces* spp.	
OTHER 5%		

- < 48 hrs of admission

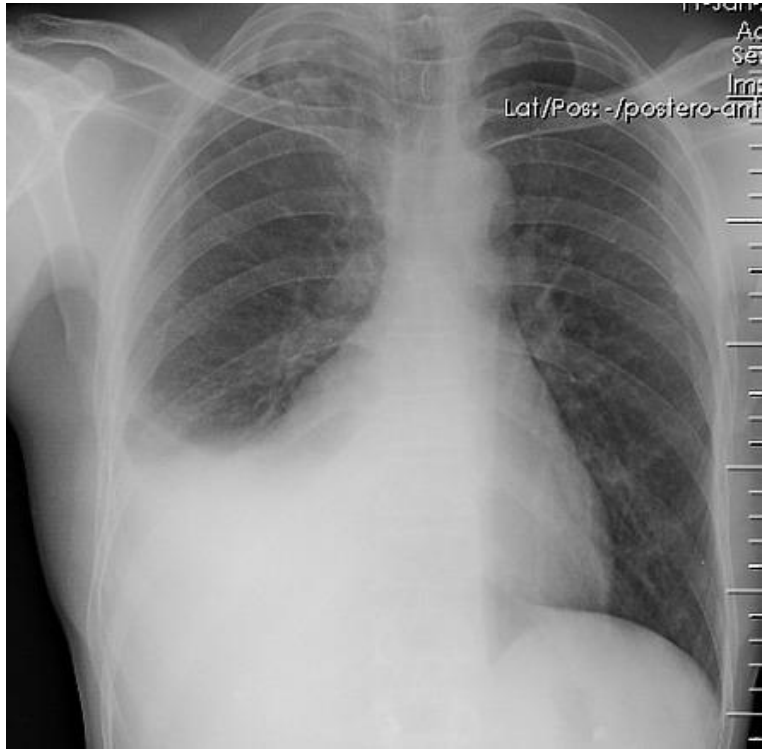
HOSPITAL ACQUIRED 15%		
AEROBES 88%	*STAPHYLOCOCCI* 40%	*MRSA* 71%
		S. aureus 29%
	GRAM NEGATIVE 26%	**'Gram negative'** includes *Escherichia coli*, Other coliforms, Proteus, *Enterobacter* spp. and *Pseudomonas aeringosa*
	STREPTOCOCCI 21%	
	ENTEROCOCCCI 13%	
ANAEROBES 8%		
OTHER 4%	**'Other'** includes *Burkholderia anthina*, *Eikenella*, *Haemophilus influenzae*, oral bacterium, *Pasterella multocida*, and *Klebsiella* spp.	

- > 48 hrs of admission
- Within 90 days of hospitalization
- After recent surgery, intubation, ICU stay or chest tube

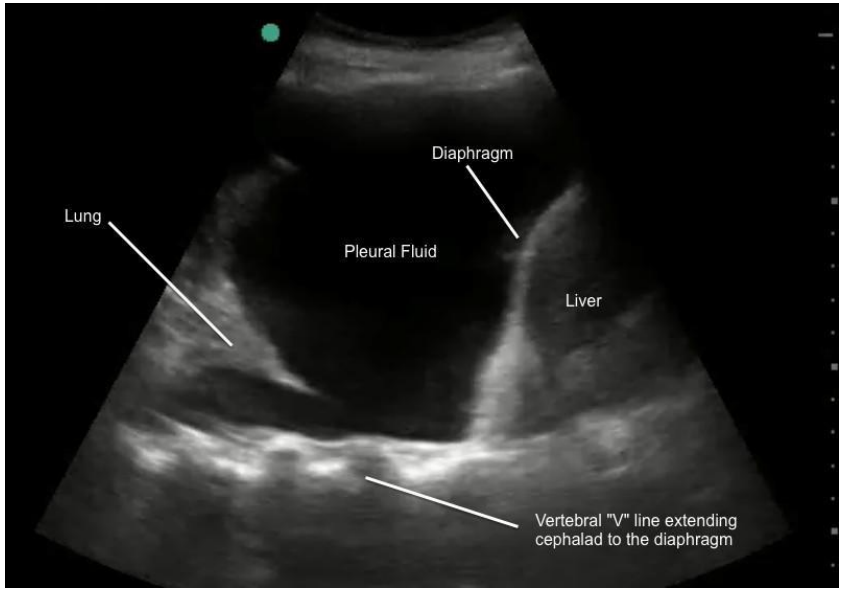
- No organism isolated in 40-50%
- Highest yield using blood culture bottles
- New: next gen sequencing increases yield



Diagnosis imaging

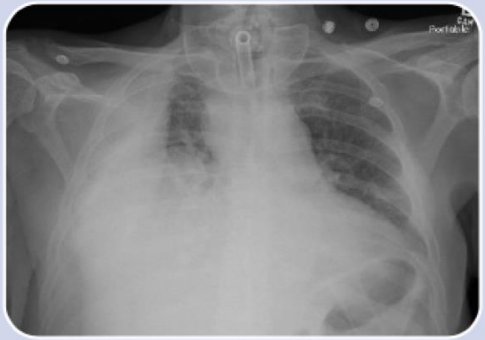


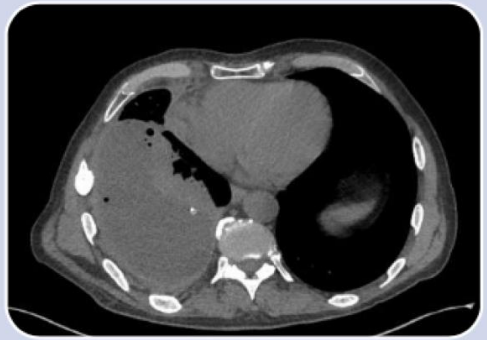




Diagnosis
Imaging







US

- Loculations
- Fine/complex
- Pleural thickening

CXR

- Pneumonia
- Loculated

CT

- Air in pleural space
- Split pleural sign
- Loculations
- Pseudotumor

Diagnosis
Pleural Fluid Analysis

PH 7.2-7.4: intermediate risk of CPPE

Biomarker	Sensitivity %	Specificity %	AUC %
pH ⩽7.20	57 (44–70)	93 (85–100)	0.83 (0.75–0.91)
Glucose ⩽60 mg·dL^{-1}	59 (46–71)	90 (82–98)	0.80 (0.72–0.88)
LDH ⩾1000 U·L^{-1}	75 (63–86)	82 (71–92)	0.82 (0.75–0.90)
CRP ⩾80 mg·L^{-1}	68 (56–79)	75 (63–87)	0.81 (0.63–0.88)
sTREM-1 ⩾180 pg·mL^{-1}	72 (61–83)	82 (71–92)	0.79 (0.70–0.86)
PCT ⩾0.25 ng·mL^{-1}	33 (21–45)	72 (59–86)	0.59 (0.49–0.70)
LBP ⩾17 µg·mL^{-1}	76 (64–87)	81 (70–92)	0.84 (0.76–0.91)

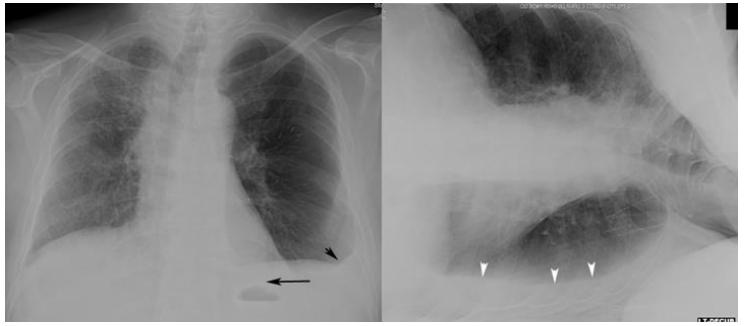
AUC: area under the curve; LDH: lactate dehydrogenase; CRP: C-reactive protein; sTREM-1: soluble triggering receptor expressed on myeloid cells-1; PCT: procalcitonin; LBP: lipopolysaccharide binding protein. Reproduced from [15] with permission.

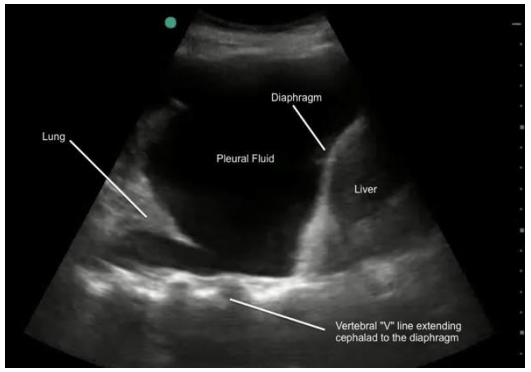
Biomarkers no conclusive evidence

Procalcitonin, CRP, inflammatory cytokines, enzymes

Porcel JM, Eur Respir J 2019
Bedawi EO, Eur Resp Rev 2021

Parapneumonic effusions
To drain or not to drain





Uncomplicated parapneumonic effusion (typically free-flowing [ie, no loculations], small to moderate size [eg, costophrenic angle blunting only, <10 mm on lateral decubitus radiograph or estimated volume <100 mL on imaging] and, if sampled, has no evidence of bacterial involvement on culture/chemistry)

↓

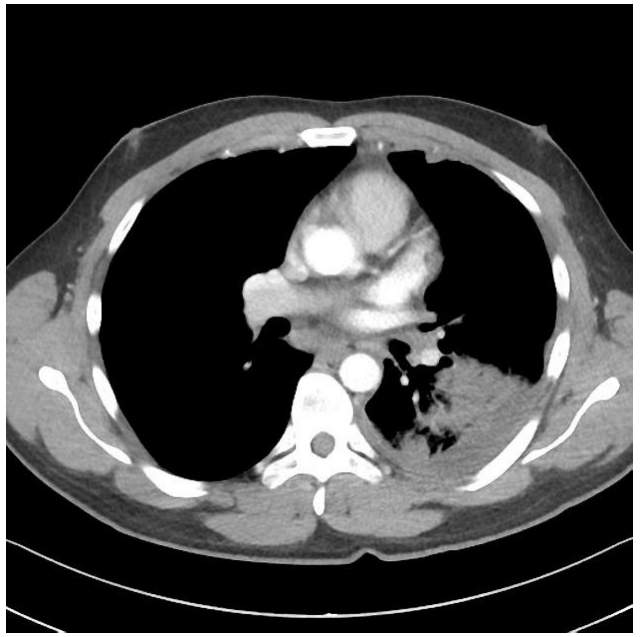
Empiric antibiotic therapy*

↓

Good clinical and radiographic response by 2 to 4 days?¶

Yes → Continue therapy and follow up as an outpatient on antibiotics

No → Investigate for the development of a complicated parapneumonic effusionΔ



Parapneumonic effusions Treatment Antibiotic therapy

- Often not adequate by itself (unless small and uncomplicated effusion)
- Should cover anaerobes
- MRSA coverage on postprocedural or hospital acquired infections
- Duration of therapy:
  - varies: clinical and radiographic improvement
  - 2-6 weeks

Empiric Tx options

- A 3rd gen cephalosporin **plus** Metronidazole
- A beta-lactam/beta-lactamase inhibitor

For PCN allergic:

- A Carbopenem
- A quinolone + Metronidazole
- A Monobactam + Mitronidazole

Treatment of Complicated effusions and Empyema

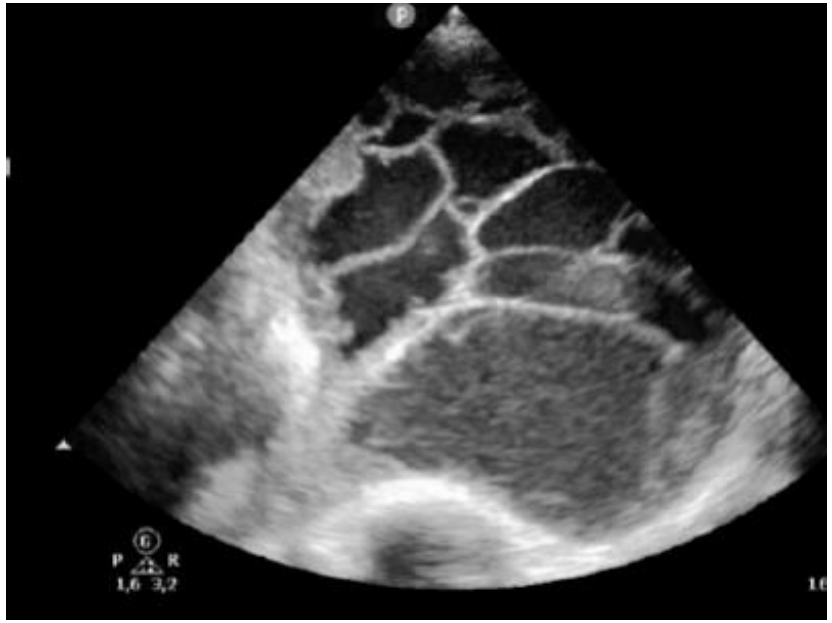
Antimicrobial therapy

Guided by culture results

Remove pleural fluid

- Pleural intervention
- Fibrinolytics/DNase
- Surgery

Eradicate Infection



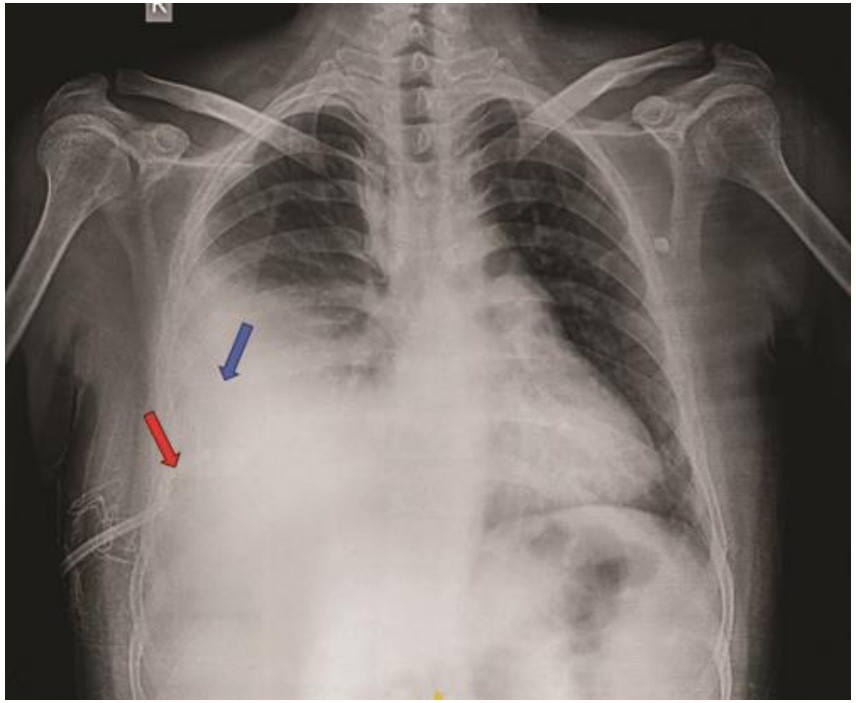
Assessment of drainage response

- CXR after tube placement and daily thereafter
- Followed clinically (signs and symptoms, labs, drainage volume)
- 24 to 48 hours
- Consider CT to assess accurate tube position and adequate drainage

When is tube drainage alone insufficient?

- Ongoing pleural sepsis (lack of source control)
- Significant residual effusion preventing re-expansion

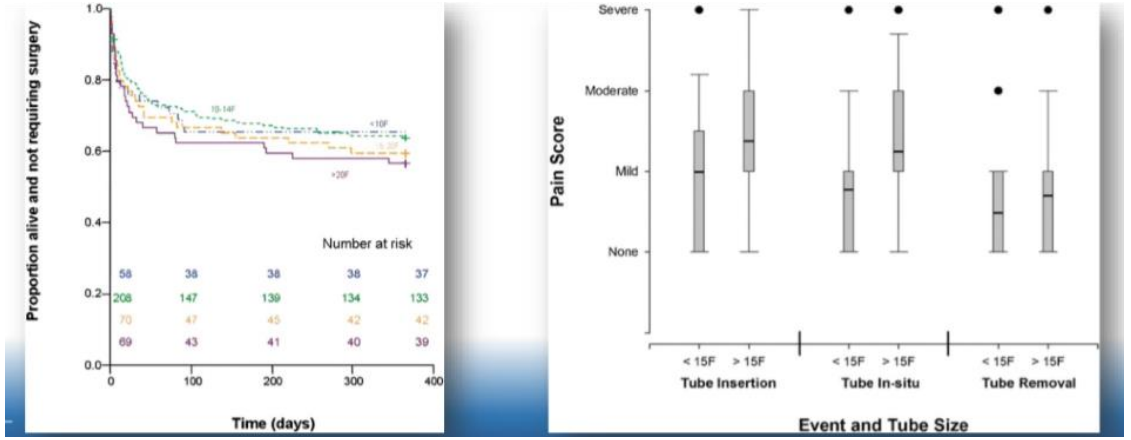
- Options
  - Intrapleural fibrinolytics: most evidence
  - Intrapleural saline lavage: not enough evidence
  - VATS
  - Medical thoracoscopy



What chest tube size is adequate?

MIST1

- 52 UK centers, n = 405 with empyema or pH <7.2
- Intervention was intrapleural streptokinase vs. placebo; no difference between groups
- Choice of chest tube left up to local physicians; all placed to -20 suction and all flushed thrice daily
- **14F and smaller equivalent to 16F and larger; more pain with larger tubes**



Which pleural fibrinolytic is more effective?

MIST 2 ORIGINAL ARTICLE

Intrapleural Use of Tissue Plasminogen Activator and DNase in Pleural Infection

Intrapleural tPA + DNase is effective
Significant reduction of x-ray opacity
Reduction of need for surgery
Shorter hospital stay

Blinded trial with 210 patients with pleural infection
Randomly assigned to 1 of 4 study treatment for 3 days, bid
Primary outcome: Change in pleural opacity on CXR day 1 to day 7
Secondary outcomes: referral for surgery, duration of hospital stay, adverse events



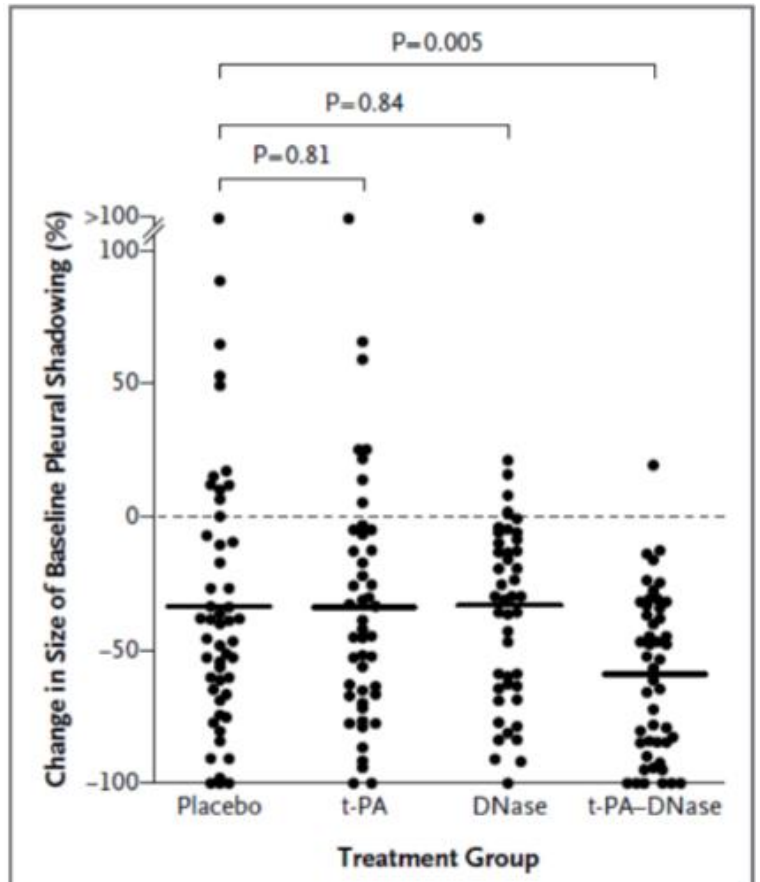


Figure 2. Change in Area of Pleural Fluid on Chest Radiography on Day 7 versus Day 1, According to Study Group.

Each circle represents an individual patient, and mean changes are indicated by the horizontal bars.

Clinical outcomes	Summary of evidence review (fibrinolytic treatment vs standard care*) (95% CI)					
(Fibrinolytic treatment)	Streptokinase	Urokinase	TPA plus DNAse	TPA	DNAse	Saline irrigation
Length of hospital stay	No difference	3.9 days shorter (5.9 to 13.7) with urokinase	Shorter with TPA plus DNAse	No difference†	No difference†	No difference†
Need for repeat intervention	No difference†	Not reported	Not enough evidence	Not reported	Not reported	Not reported
Need for thoracic surgery	No difference	Reduced need with urokinase (230/1000 (123 to 435) compared with 512/1000)¶	Reduced need with TPA plus DNAse†	Reduced need with TPA†	No difference†	Reduced need with saline irrigation†
Patient symptoms‡	Reduced symptoms with streptokinase†	Defervesence achieved 4.2 days faster (0.4 to 7.9) with urokinase	Reduced symptoms with TPA plus DNAse†	No difference†	No difference†	No difference†
Complications§	Increased with streptokinase (114/1000 (64 to 205) compared with 46/1000)¶	Not reported	Inconclusive results	Inconclusive results	Inconclusive results	No difference†
Quality of life	Not reported	Not reported	Not reported	Not reported	Not reported	Not reported
Mortality	No difference	Not reported	No difference†	No difference†	No difference†	No difference†
Radiological opacification	Inconclusive results	Increased resolution with urokinase†	Increased resolution with TPA plus DNAse†	No difference†	No difference†	Increased resolution with saline irrigation†
Radiographic resolution of effusion	No difference	Greater resolution with urokinase†	Greater resolution with TPA plus DNAse†	Greater resolution with TPA†	Not reported	Not reported
Pleural thickening	No difference†	Potential reduced pleural thickening with urokinase†	Not reported	Not reported	Not reported	Not reported

Use of fibrinolytics and deoxyribonuclease in adult patients with pleural empyema: a consensus statement

Udit Chaddha*, Abhinav Agrawal*, David Feller-Kopman, Viren Kaul, Samira Shojaee, Fabien Maldonado, Mark K Ferguson, Kevin G Blyth, Horiana B Grosu, John P Corcoran, Ashutosh Sachdeva, Alex West, Eihab O Bedawi, Adnan Majid, Ravindra M Mehta, Erik Folch, Moishe Liberman, Momen M Wahidi, Sidhu P Gangadharan, Mark E Roberts, Malcolm M DeCamp, Najib M Rahman

The Lancet Respiratory Medicine
Volume 9, Issue 9, September 2021, Pages 1050-1064

- Avoid fibrinolytic monotherapy
- Use combination fibrinolytic + Dnase
- Suggest 5 mg DNase and 10 mg tPA twice daily (**BTS: half tPA dose if bleeding concern)
- Suggest concurrent administration of tPA/Dnase
- Clamp tube for at least 1 hour
- Individualized number of doses based on clinical/radiographic response
- Hold antiplatelet/anticoagulants before starting tPA/DNase if possible; avoid use in systemic coagulopathy
- Stage 2: suggest tPA/DNase first; Stage 3: consider upfront VATS if expertise is available
- No compelling evidence re: comparative cost effectiveness of tPA/DNase vs. upfront VATS
- Suggest pleural irrigation only in patients with contraindications to lytics and surgery

Intrapleural fibrinolytic protocol

- Flushed tube with 10 cc saline
- Instill tPA
- Flush with 10 cc saline
- Instill DNAse
- Flush with 10 cc saline
- Clamp for 1 hour: turn patient
- Unclamp after 1 hour
- Max: BID X 3 days

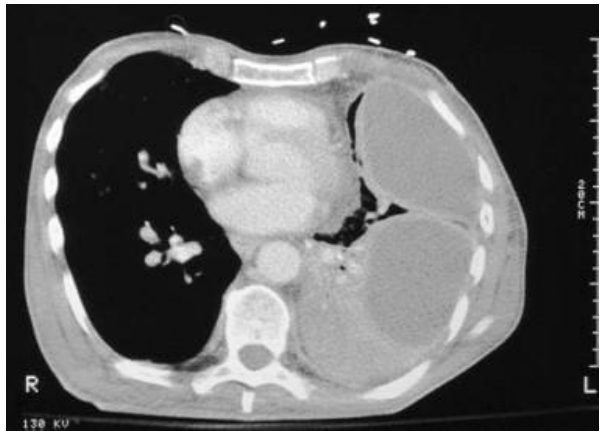


Side effects of intrapleural fibrinolytics

- Chest pain
- Fever
- Allergic reactions (more frequent with streptokinase)
- Pleural hemorrhage:
  - Around 7%
  - Most worrisome: blood loss and lung entrapment
  - Highest risk if other risks of bleeding (eg, renal failure, thrombocytopenia, anticoagulation)
  - Requires VATS
- Systemic bleeding is rare
  - fibrinolytics are quickly neutralized (usually within an hour) by plasminogen activator inhibitors that are increased during pleural infection

Additional drainage tubes

- When drainage is inadequate with one chest tube
  - Multiloculated effusions
  - Failure of fibrinolytic therapy
- Often CT-guided
- More likely to succeed in small number of locules (2-3)
- Unlikely to work if multiple locule(s), locules along the mediastinal pleura or interlobar fissures.
- Lung parenchymal abscesses should not be drained percutaneously



When to remove the chest tube

- Drainage < 50 to 100 mL/day
- Reasonable size reduction of the effusion
- Resolving or No signs of clinical infection

- Complete resolution of pleural thickening not required
- Follow up imaging in office

Surgical approach

- After chest tube + fibrinolytic failure
- Consider early if:
  - unstable patient, or
  - stage III / organized / thick rind (usually >4 wks symptoms)
- VATS preferred over open thoracotomy
  - Often with decortication
  - Conversion from VATS to open thoracotomy 10% up to 44%

VATS vs chest tube drainage

- Data is mixed
- Several small series suggested that thoracoscopy is superior to intrapleural fibrinolysis
- Meta-analysis of 7 randomized trials:
  - No difference in mortality
  - VATS resulted in a reduced length of hospital stay

Summary of findings 2. VATS compared to thoracostomy drainage for pleural empyema

VATS compared to thoracostomy drainage for pleural empyema

Patient or population: children and adults with pleural empyema
Intervention: VATS
Comparison: thoracostomy drainage

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Quality of the evidence (GRADE)	Comments
	Thoracostomy drainage	VATS				
Mortality	Risk in study population		**OR 0.80** (0.04 to 14.89)	361 (7 RCTs)	⊕⊖⊖⊖ LOW[1]	Data only for adults
	6 per 1000	**5 per 1000** (0 to 78)				
Mortality: children	Risk in study population		Not estimable	271 (5 RCTs)	⊕⊕⊕⊖ MODERATE [2]	No deaths occurred in either group.
	Not pooled	Not pooled				
Mortality: adults Follow-up: not reported	Risk in study population		**OR 0.80** (0.04 to 14.89)	90 (2 RCTs)	⊕⊕⊕⊖ MODERATE [3]	No deaths occurred in Bilgin 2006. Data based on Wait 1997
	23 per 1000	**18 per 1000** (1 to 257)				
Length of hospital stay (days) Follow-up: 1 year in Cobanoglu 2011 and 3 months in Marhuenda 2014	Control group	The mean length of hospital stay in the intervention group was **2.52 days fewer** (4.26 fewer to 0.77 fewer).	—	231 (5 RCTs)	⊕⊕⊕⊖ MODERATE[4]	Note: Follow-up period not reported in Kurt 2006; Peter 2009; Wait 1997.
Procedural complications Follow-up: 6 months in Bilgin 2006 and not reported in Wait 1997	Risk in study population		**OR 0.46** (0.08 to 2.75)	271 (5 RCTs)	⊕⊕⊕⊖ MODERATE [5]	
	23 per 1000	**11 per 1000** (2 to 60)				

***The risk in the intervention group** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
CI: confidence interval; **OR:** odds ratio; **RCT:** randomised controlled trial; **VATS:** video-assisted thoracoscopic surgery

GRADE Working Group grades of evidence
High quality: We are very confident that the true effect lies close to that of the estimate of the effect.

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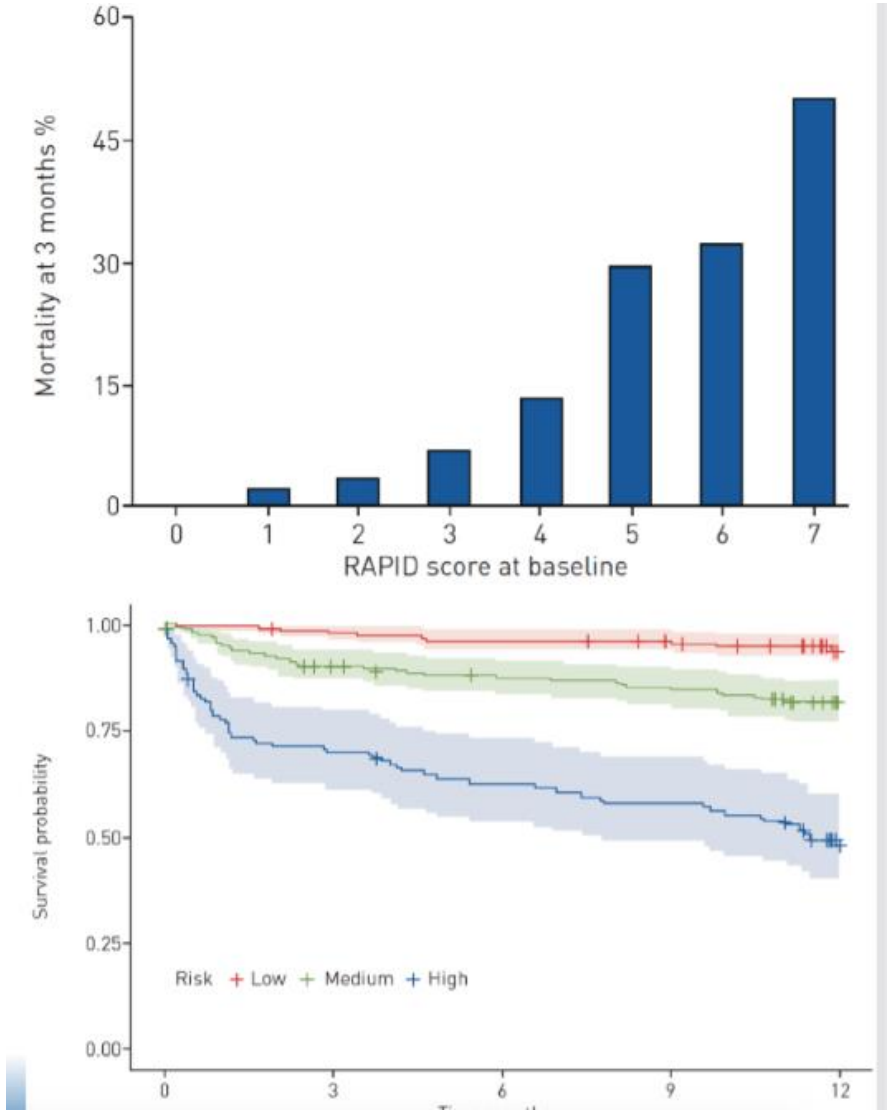
Cochrane Database of Systematic Reviews

Prognosis of parapneumonic effusions: RAPID score

TABLE 1 The RAPID risk-prediction score, using baseline clinical parameters in patients with pleural infection [30]

Parameter	Score
Renal (urea) mmol·L^{-1}	
<5.0	0
5.0–8.0	1
>8.0	2
Age years	
<50	0
50–70	1
>70	2
Purulence of pleural fluid	
Purulent	0
Non-purulent	1
Infection source	
Community-acquired	0
Hospital-acquired	1
Dietary factor (albumin) g·L^{-1}	
⩾27.0	0
<27.0	1
Risk category	
Low	0–2
Medium	3–4
High	5–7



Tuberculous pleural effusion

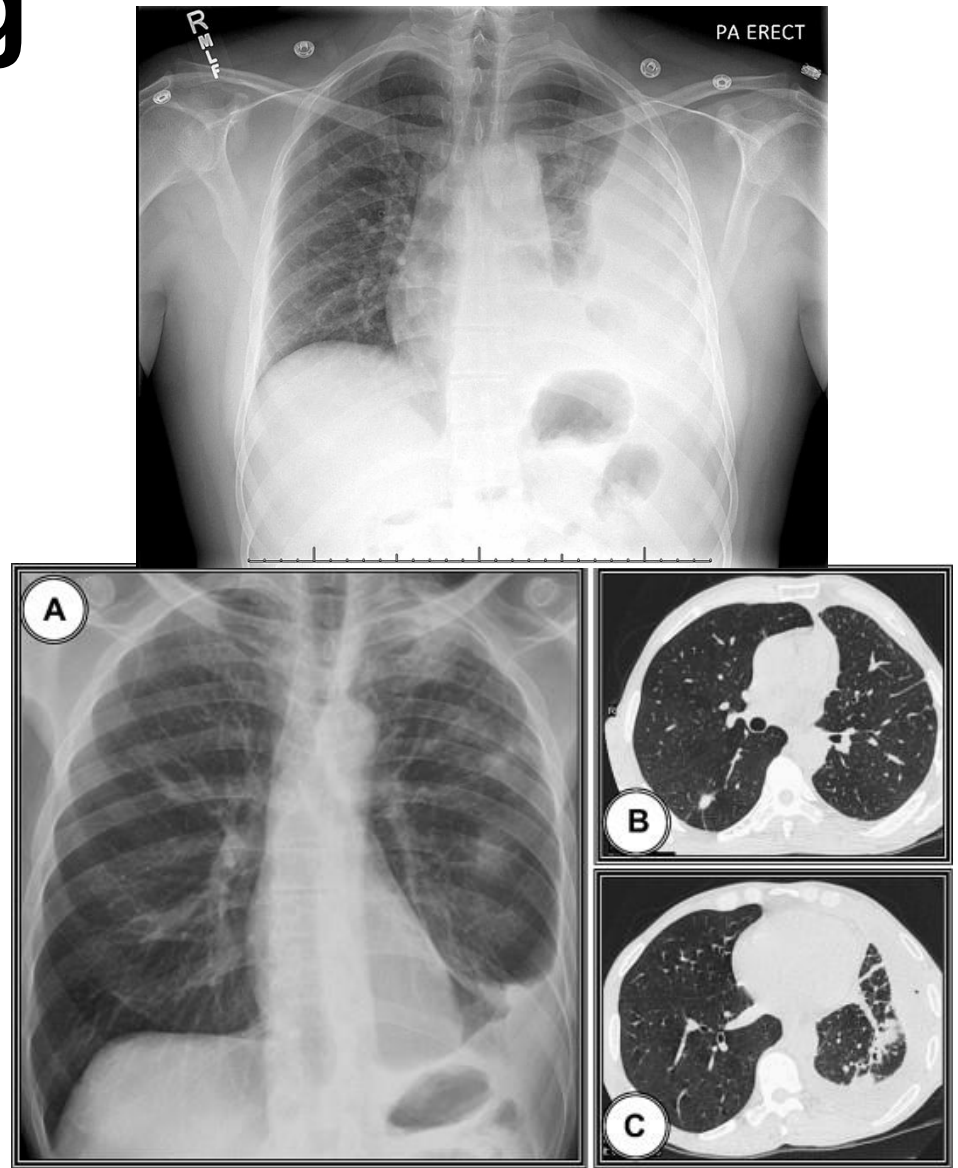
- Primary tuberculous or reactivation disease
- In adults, often reactivation disease
- In children, often primary disease
- Mechanism:
  - Delayed hypersensitivity reaction to mycobacteria or mycobacterial antigens in the pleural space in sensitized individuals
  - Rupture of a subpleural focus of pulmonary disease into the pleural space

Tuberculous pleural effusion signs and symptoms

- Usually acute
- Fever and nonproductive cough (94 %)
- Pleuritic chest pain (78 %)
- Night sweats, chills, weakness, dyspnea, and weight loss
- WBC typically normal
- Patients with HIV are at increased risk

Tuberculous pleural effusion Imaging

- Usually unilateral
- Right side 55%
- Upper lobe involved 75% (Reactivation)
- Lower lobe involved 25% (primary)
- 10-15% Miliary pattern and adenopathy (HIV pts)
- CT: parenchymal disease 40- 80%
- Indistinguishable from non TB effusions
- **Maintain high clinical suspicion by history**



Tuberculous pleural effusion Diagnosis

- Straw colored
- Protein >3.0 g/dL (30 g/L)
- LDH: Elevated in75%, commonly >500 iu/L
- PH <7.40 in most cases; <7.30 in 20%
- Glucose: Usually between 60 and 100 mg/
  - < 50 mg/dL in 7-20%
- Neutrophilic early on, then Lymphocytic 60-90%
- Lymphocyte/Neutrophil ratio > 0.75

***Pleural effusion Exudate, low glucose, lymphocytic predominant (10% N predominant)**
<5% mesothelial cells
ADA elevated

***If confirmed, HIV test**

Tuberculous pleural effusion
Pleural fluid AFB culture

- Non- HIV: < 20 to 30%
- HIV: 50 % (esp with low CD4 counts)
- Tuberculous empyema fluid is grossly purulent and usually AFB smear and culture positive

Tuberculous pleural effusion Sputum AFB smear and culture

- Sputum culture positive 20-50% :
  - With concomitant parenchymal disease 80%+
  - Without concomitant parenchymal disease only 11%

Tuberculous pleural effusion
Pleural Fluid Adenosine Deaminase (ADA)

- Cutoff is variable
- ADA > 60 u/L : sensitivity and specificity in the 90s% in the correct clinical setting
- Nonspecific:
  - Bacterial parapneumonic effusions and empyema, mesothelioma, lung cancer, lymphoma
  - ADA-2 more TB specific, ADA-1 other causes, but most assays do not distinguish

Tuberculous pleural effusion
Pleural Fluid Adenosine Deaminase (ADA)

- Diagnostic performance is affected by the local prevalence of TB
  - In low prevalence regions: very high negative predictive value.
  - In high prevalence regions:
    - Low negative predictive value
    - ADA levels >70 U/L = Very high diagnostic probability
    - ADA level 40 to 70 U/L: probability depends upon the pretest probability of TB
- Higher diagnostic yield in HIV patients

Tuberculous pleural effusion
Other Pleural Fluid tests

MTB PCR Nuclear Acid Amplification (NAA) assay:

- Off label use: Not approved for use with pleural fluid in the US
- High specificity (99%) but low sensitivity (49%) in non HIV pts

Pleural fluid interferon-gamma concentration

- not been approved by the FDA

Pleural fluid lysozyme concentrations

- not been approved by the FDA

PF Interferon-gamma release assays (IGRAs) “QuantiFERON” or T-SPOT

- In one metanalysis: Sensitivity 72%, specificity 77%

Combining both PF T-SPOT and PF IFN-g : > 90% (one study in China)

Tuberculous pleural effusion
TST and IGRAs

TST:

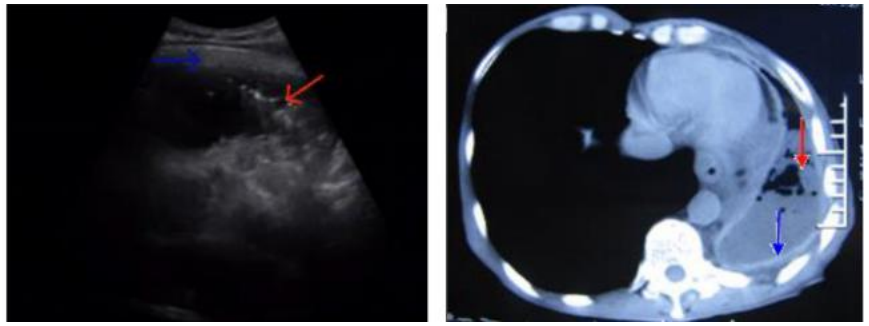
- Cannot distinguish latent from active TB
- Cannot distinguish BCG vaccinated from infected
- Falsely negative 7-30%
- May turn from negative to positive later on (2 months)

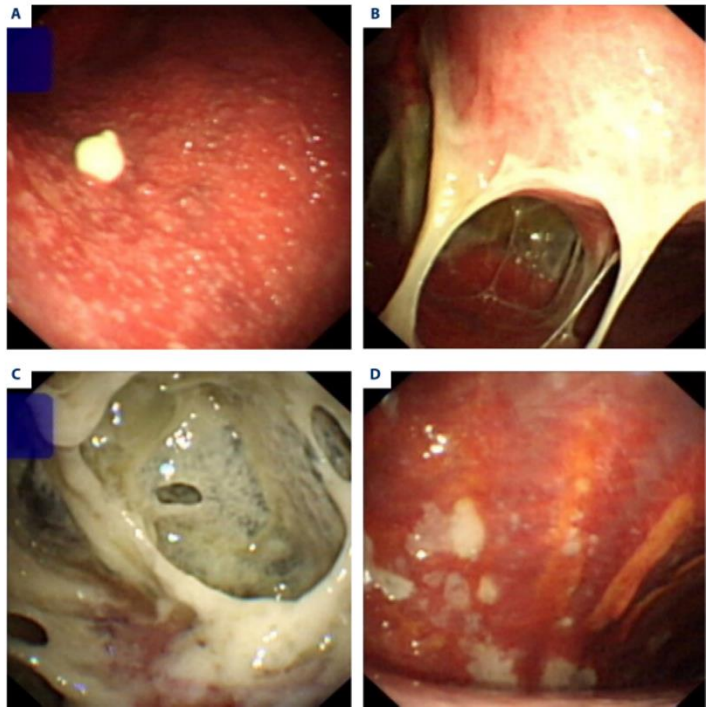
Blood IGRAs:

- QuantiFERON and T-SPOT
- Sensitivity 77%
- Specificity 71%
- Preferred in BCG vaccinated individuals
- Pleural IGRA higher yield but not FDA approved

Tuberculous pleural effusion
Pleural biopsy

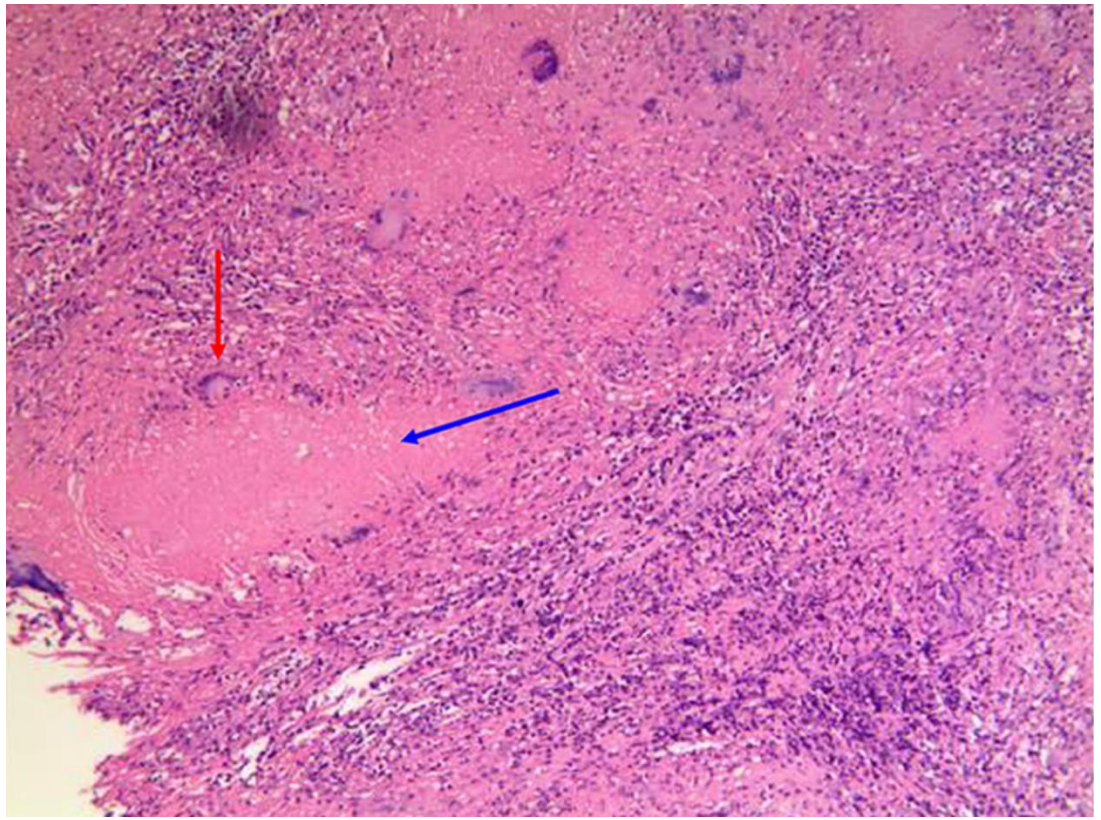
- Clinical suspicion + pleural fluid is suggestive + ADA level is <40-70 u/L
- If drug resistance is suspected, for sensitivities
- Blind, Image guided or thoracoscopic





Tuberculous pleural effusion
Pleural biopsy

- Overall yield 60-95%
- Granulomas 50-97%
  - +/- necrotizing (diagnostic)
  - +/- acid-fast bacilli
- Culture 40 - 80 % positive



Ultrasound-Guided versus Thoracoscopic Pleural Biopsy for Diagnosing Tuberculous Pleurisy Following Inconclusive Thoracentesis: A Randomized, Controlled Trial

© Med Sci Monit, 2018; 24: 7238-7248
DOI: 10.12659/MSM.912506

- RCT
- 196 pts with suspect pleural TB
- Exudative effusion, -ive AFB, ADA < 70
- Flex thoracoscopy Vs US-pleural bx

Diagnosis	Ultrasound group, n (%)	Thoracoscopy group, n (%)
Tuberculous pleurisy	65 (66%)	62 (63%)
Metastatic malignancy	18 (18%)	22 (22%)
Emphysema	4 (4%)	6 (6%)
Non-specific inflammation	7 (7%)	2 (2%)
Lymphoma	2 (2%)	0 (0%)
Mesothelioma	2 (2%)	4 (4%)
Indeterminate	0 (0%)	2 (2%)

Pleural thickness	Ultrasound group sensitivity	*P*-value*	Thoracoscopy group sensitivity	*P*-value*
≥1 cm	94% (34/36)	0.06	94% (32/34)	0.57
<1 cm	66% (19/29)		86% (24/28)	

Complication	Ultrasound groupn (%)	Thoracoscopy group, n (%)
Chest pain	6 (6%)	18 (18%)
Fever	10 (10%)	6 (6%)
Subcutaneous emphysema	0 (0%)	20 (20%)
Pneumothorax	4 (4%)	0 (0%)
Hemoptysis	8 (8%)	4 (4%)
Wound empyema/infection	0 (0%)	2 (2%)

In summary
Diagnosis of pleural TB

- **Clinical suspicion**
  - Epidemiologic risk factors/exposure
  - Positive TST or IGRA (IGRA in BCG vaccinated)
- **Definitive Dx:**
  - MTB in pleural fluid or a pleural biopsy specimen (may take weeks)
- **Presumptive**
  - High clinical suspicion + PF lymphocytic-to-neutrophil ratio >0.75 and ADA >40 units/L OR
  - High clinical suspicion + One or more caseating granulomas on pleural biopsy
- Test for pulmonary TB especially if + parenchymal disease

In summary
Diagnosis of pleural TB

Indications for pleural biopsy in suspected pleural TB

- Pleural fluid ADA level is <40 units/L and/or pleural fluid evaluation is otherwise not diagnostic.
- Drug susceptibility data are needed

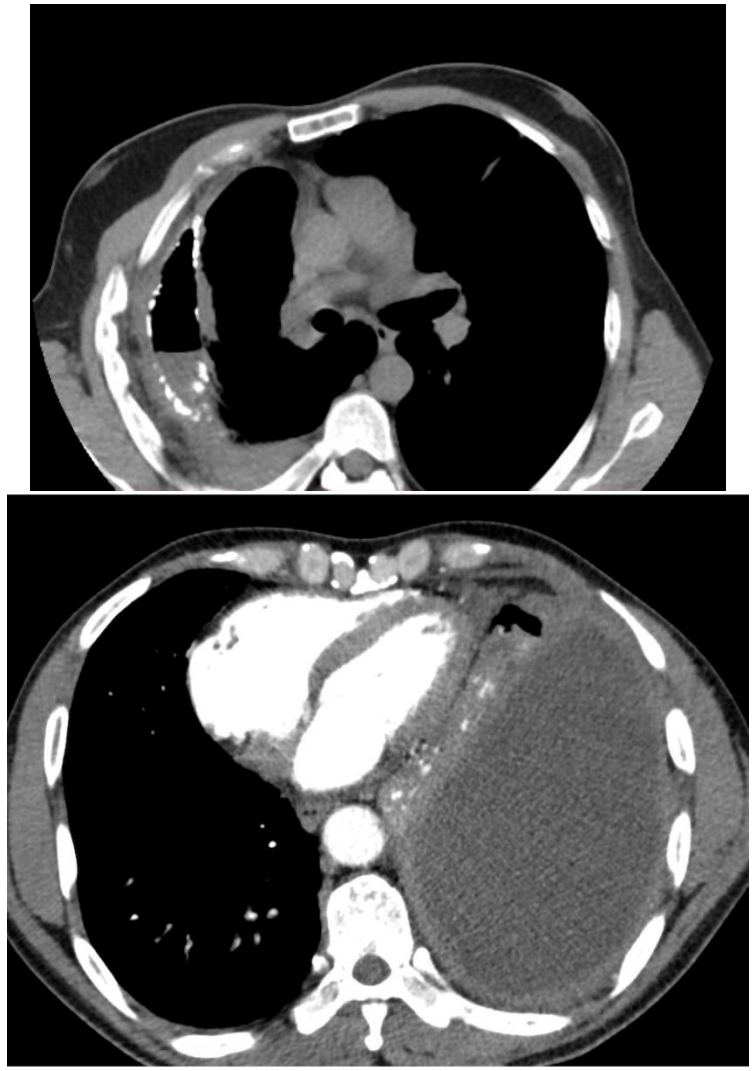
Presence of caseating (necrotizing) granulomas on histologic examination is virtually diagnostic

Tuberculous pleural effusion Complications

- TB Empyema
- Tuberculous empyema necessitans
- Pleuro-cutaneous fistula
- Psuedochylothorax

Tuberculosis empyema

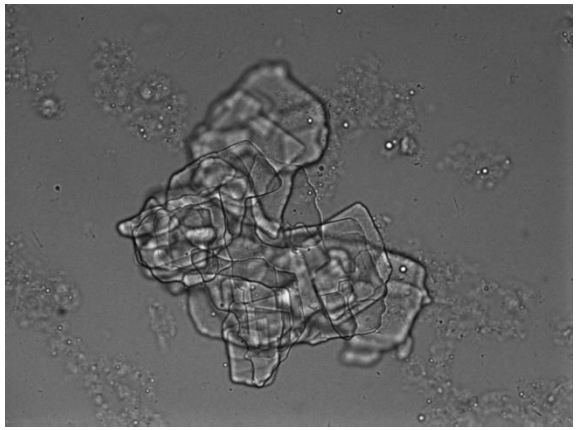
- Thick +/- calcified pleura
- Neutrophilic predominant
- High mycobacterial burden (higher yield for smear/cx)
- Invasive surgery is often required



Pseudochylothorax

- Cholesterol effusion
- TB is most common cause (RA, paragonimiasis)
- PF Cholesterol = or > 200 mg/dL
- PF TG < 110 mg/dL
- Cholesterol/TG ratio >1 (most sensitive)
- Cholesterol crystals rare but pathognomonic
- Treatment: serial thoracentesis, chest tube and pleurodesis, VATS decortication





Empyema necessitans



Pleuro-cutaneous fistula



Management of Pleural TB

Antituberculous therapy

- Same as active TB
- Presumptive diagnosis and treatment is warranted in epidemiologic risk factors or endemic areas
- Resolution of fever in two weeks
- Resolution of pleural effusion in six weeks
  - If these are not observed, further considerations include drug-resistant TB or alternative diagnosis.

No role for routine steroid use

- Insufficient data
- Some old data: steroids may shorten the duration of fever and time to resorption
- No difference in mortality
- In Cochrane analysis, the long-term impact of steroids is uncertain

Management of Pleural TB

Pleural drainage

- Therapeutic thoracentesis is reasonable for symptom relief
- Routine complete drainage with chest tube or catheter does not appear to affect long-term outcomes
- Data for tPA +DNAse in TB effusions are insufficient
  - Some studies have demonstrated lower incidence of residual pleural thickening and higher lung volumes
- Tuberculous empyema often require decortication

Management of Pleural TB
Follow up and Prognosis

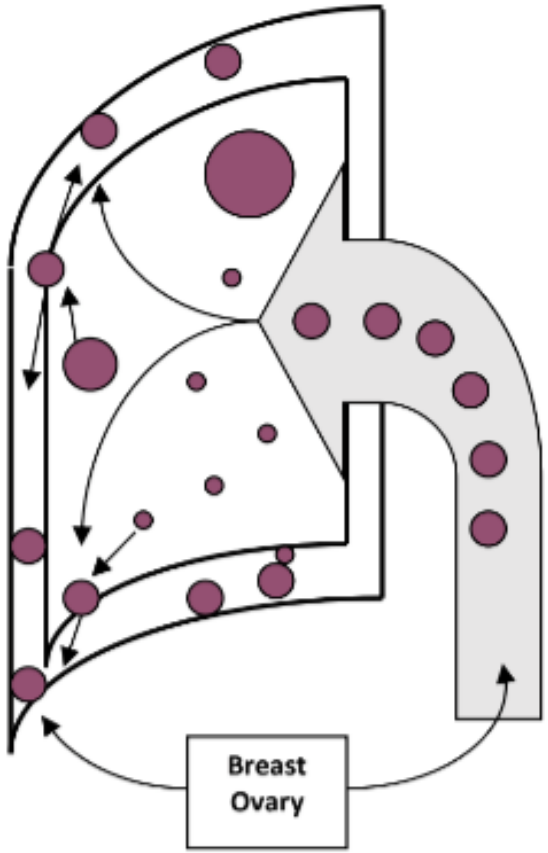
- Most patients defervesce within two weeks, up to 2 months
- Pleural fluid is resorbed within six weeks, up to 4 months.
- In HIV patients: immune reconstitution inflammatory syndrome if when starting ARTs

Malignant Pleural effusions

Pathogenesis of pleural metastasis

- Visceral or Parietal pleura
- Vascular embolization or direct invasion

- Primary tumors
  - Lung and breast 50 to 65%
  - Lymphomas, GU and GI 25%
  - Mesothelioma: rare, asbestos exposure



Malignant Pleural Effusions Symptoms

- Dyspnea
- Orthopnea
- Cough

Mechanisms for dyspnea

Decreased ipsilateral lung volume
V/Q mismatch
Decreased compliance-chest wall, diaphragm etc.
Contralateral shift
Neurogenic reflexes

Malignant Pleural effusions Diagnosis

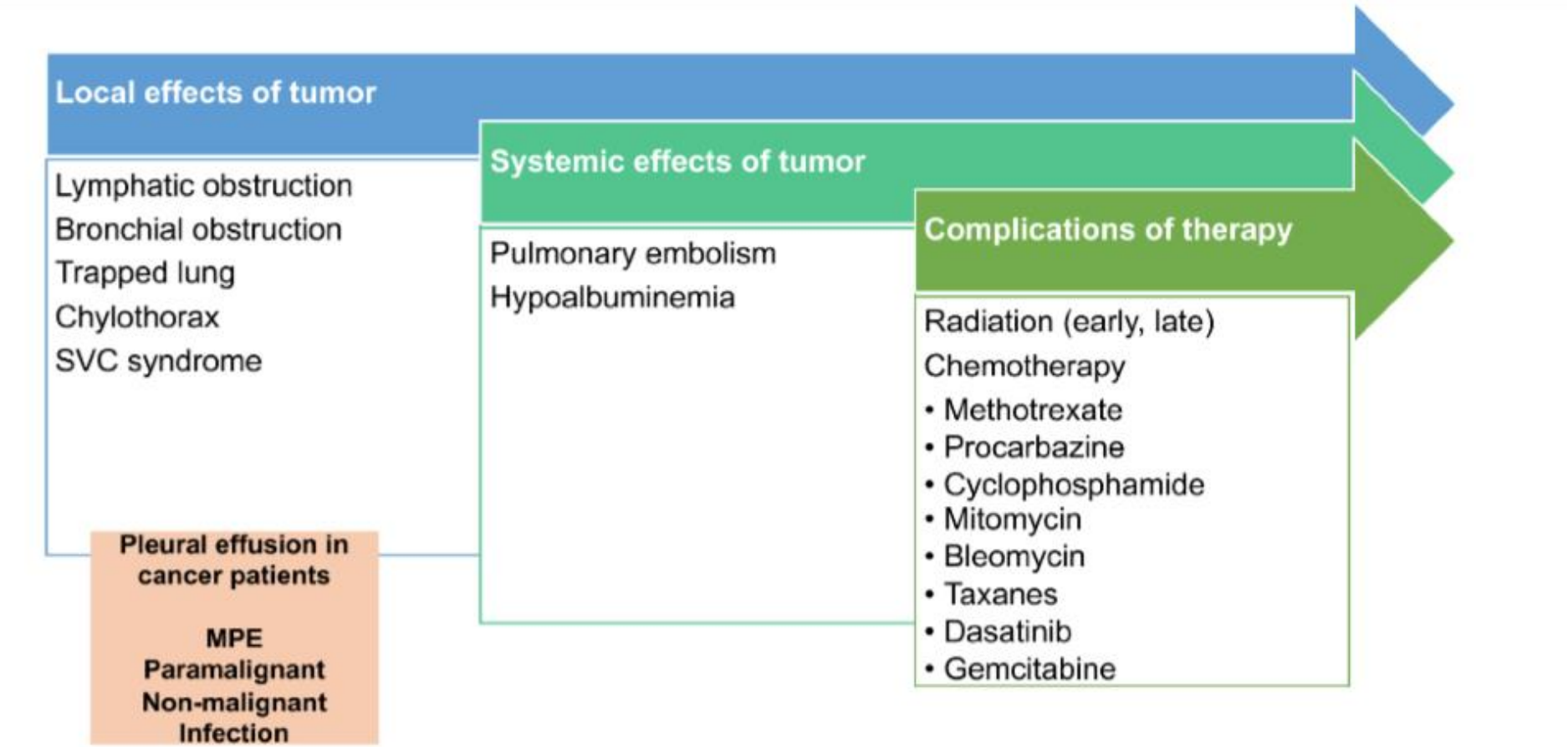
- 95% exudates
- Not every effusion in cancer patient is malignant:
  - 17% “paramalignant”
- Immunohistochemical markers not widely used

Pleural fluid studies for MPE

TABLE 2 Immunohistochemical markers with high specificity for differentiating tumour types in malignant pleural effusion

Mesothelial markers	Adenocarcinoma markers	Squamous-cell carcinoma markers	Organ-specific markers
Calretinin CK5/6 D2-40 (podoplanin) WT-1	CEA B27.3 Bg8 BerEP4 MOC-31	P40 P63 CK5/6	Lung: TTF-1, Napsin A Prostate: PSA, PSMA Kidney: PAX-2, PAX-8, RCC, CAIX Pancreas: CA 19-9 Gastrointestinal: CDX-2, CK20 Gynaecological: PAX-8, WT1 Breast: Mammaglobin, GCDFP-15, ER, PR, GATA3

Paramalignant Pleural Effusions

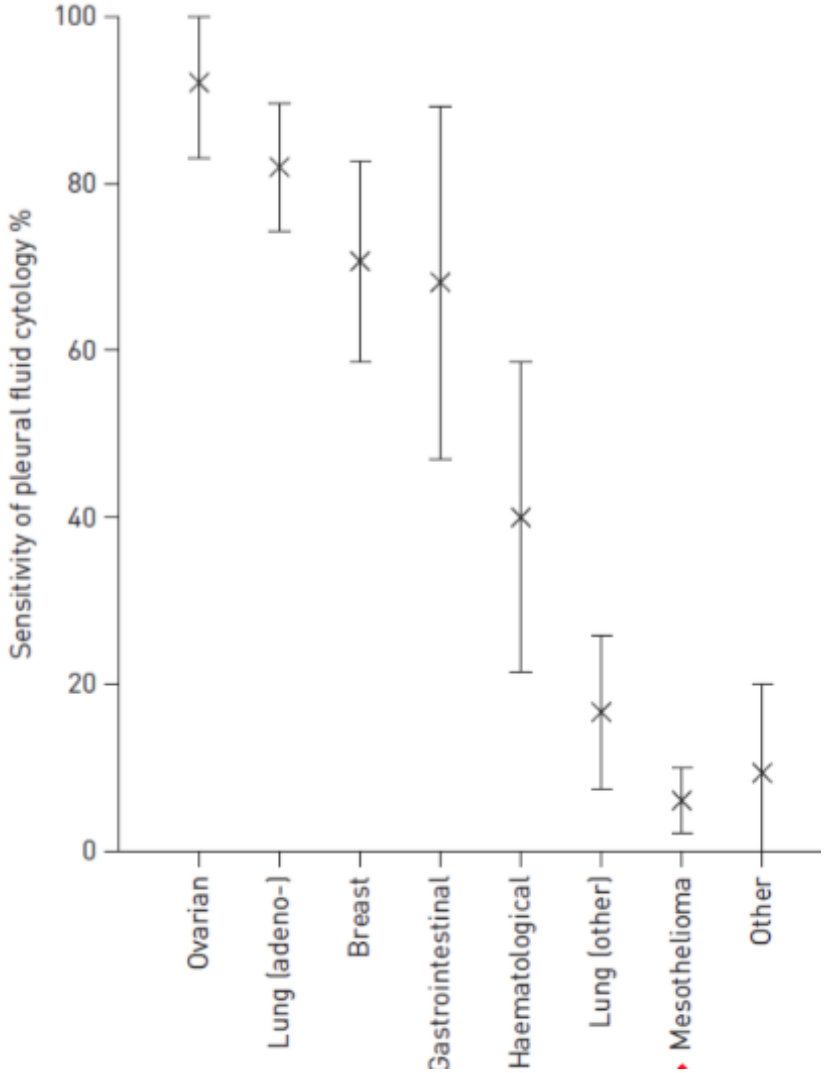


Malignant Pleural effusions Diagnosis

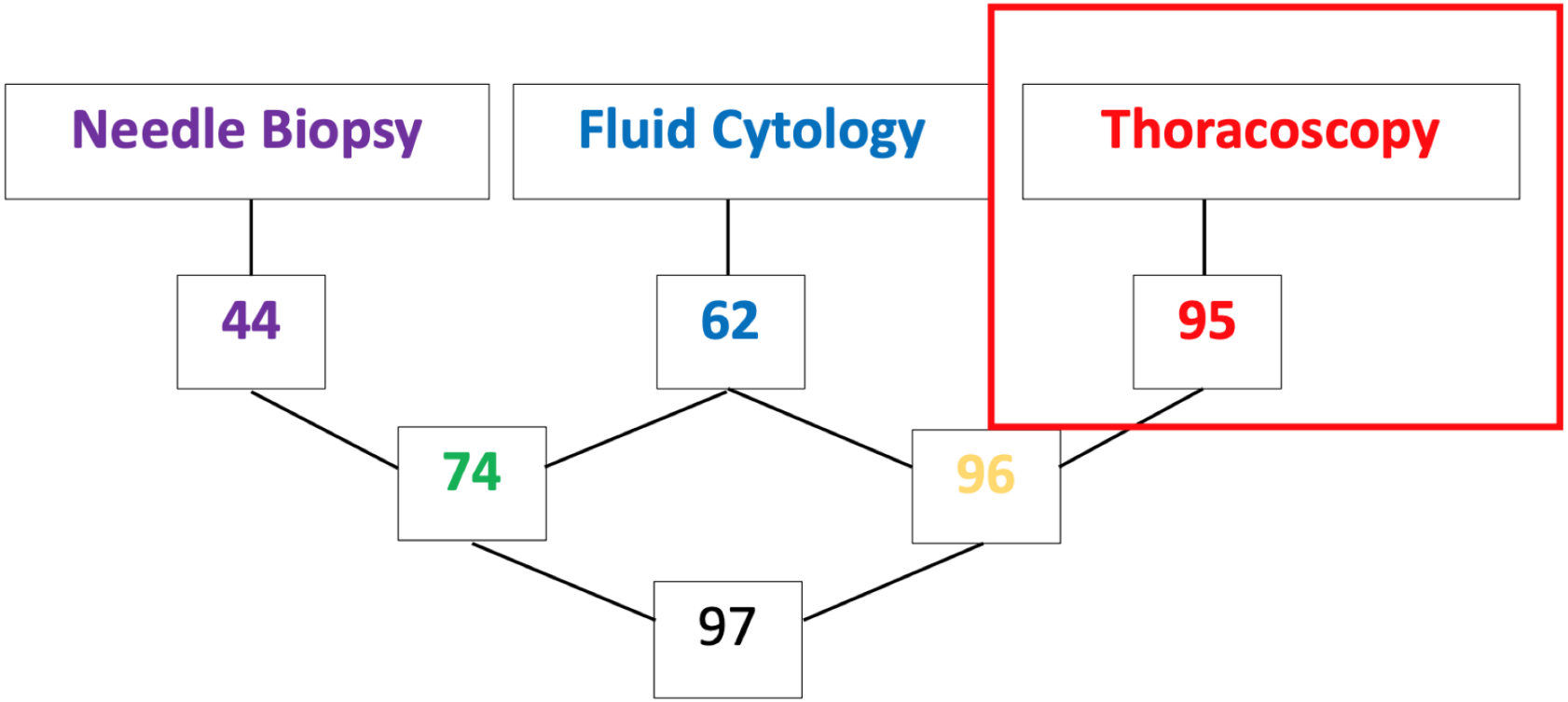
Pleural fluid cytology

- Sensitivity widely vary 40 to 87%
- 60% on initial thoracentesis sample, Increases by about 15-20% with a 2nd sample, maybe another 10% with a 3rd sample then does not increase
- Sensitivity varies by tumor type

- Flow cytometry in hematologic cancers



Malignant Pleural effusions Diagnosis



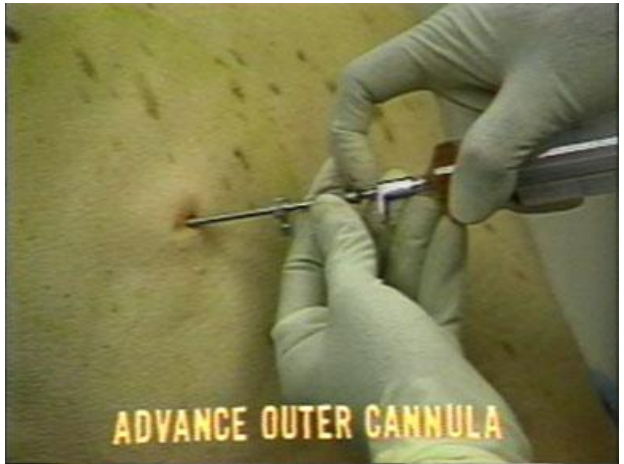
Malignant Pleural effusions
Diagnosis

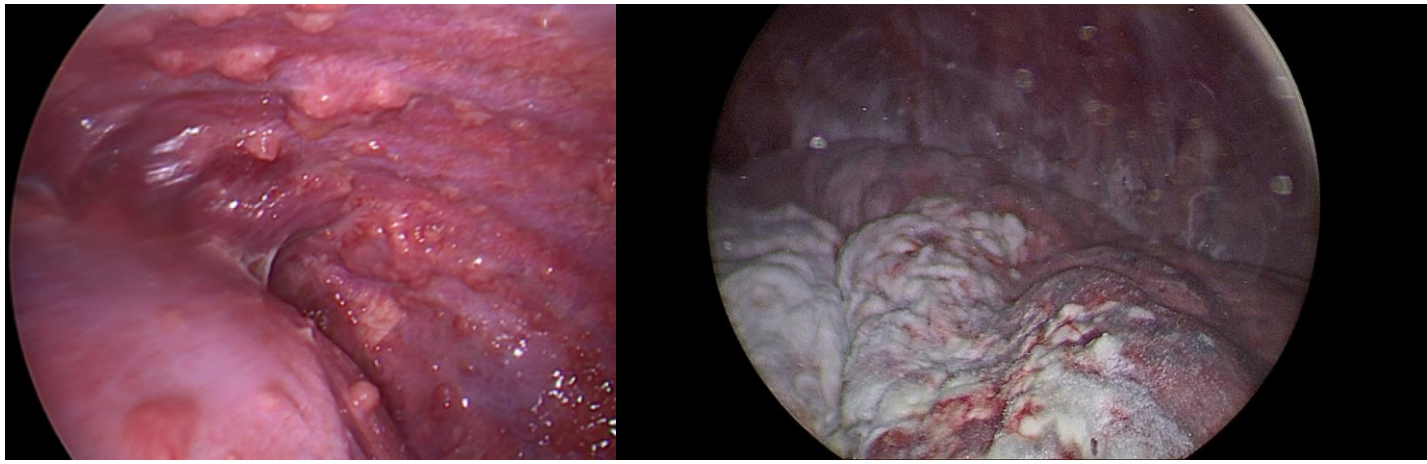
Closed Pleural Biopsy

- Core or Abrams needle
- +/- US or CT guidance
- Diagnostic yield variable
  - 70-90% reported with guidance
  - 45% blind

Pleuroscopy/VATS

- Diagnostic + Therapeutic w/ pleurodesis +/- indwelling pleural catheter
- Diagnostic yield 95%





Malignant Pleural Effusions
Impact and prognosis

- Worse prognosis
- Survival 3 to 12 months
- Significant morbidity and cost
  - > 125,000 hospital admissions/yr (US)
  - charges of > $5 billion/year (US)

Malignant Pleural Effusion Prognostication criteria

Table 3 The LENT score calculation

	Variable	Score
L	LDH level in pleural fluid (IU/L)	
	<1500	0
	>1500	1
E	ECOG PS	
	0	0
	1	1
	2	2
	3–4	3
N	NLR	
	<9	0
	>9	1
T	Tumour type	
	Lowest risk tumour types	0
	▶ Mesothelioma	
	▶ Haematological malignancy	
	Moderate risk tumour types	1
	▶ Breast cancer	
	▶ Gynaecological cancer	
	▶ Renal cell carcinoma	
	Highest risk tumour types	2
	▶ Lung cancer	
	▶ Other tumour types	

Risk categories	Total score
Low risk	0–1
Moderate risk	2–4
High risk	5–7

ECOG PS, Eastern Cooperative Oncology Group performance score; LDH, lactate dehydrogenase; NLR, neutrophil-to-lymphocyte ratio.

Malignant Pleural Effusion Treatment

Goals

Symptom relief
Prevention of fluid reaccumulating
Minimization of invasive procedures

Local therapy

Thoracentesis

Chest tube, chemical pleurodesis
Thoracoscopic, chemical/mechanical pleurodesis
Indwelling pleural catheter

Pleuro-peritoneal shunting

Pleurectomy (decortication)

Radiation therapy

Systemic therapy

Targeted therapy
Chemotherapy
Immunotherapy
Stem cell transplant

Oxygen

Palliation
Opioids
Hospice

Malignant Pleural Effusion
Treatment considerations

- Is there a confirmed diagnosis or not? → consider thoracoscopy
- Size of effusion? → can leave small effusions alone
- Symptomatic or not? → can leave asymptomatic effusions alone (unless diagnosis is essential to staging)
- Symptom relief after initial drainage or not? → if no relief, consider other causes of dyspnea and do not pursue further treatments
- Lung re-expansion after initial drainage? → No expansion = less successful pleurodesis
- Overall prognosis/longevity ? → < 1-2 months: serial thoracentesis
  → > 2-3 months: pleurodesis or IPC

Malignant Pleural Effusion
Drainage options

Pleural intervention	Pros	Cons
Thoracoscopy with talc poudrage	Can combine dx with tx Can do mini-decortication	Performing surgery in patient with advanced disease Cost
Chest tube with talc slurry	Less invasive than surgery Pleurodesis rate 70 to 95%	Hospitalization 3 to 5 d 15% require additional pleural procedures
IPC	Outpatient procedure Less need for further intervention	Need to manage catheter Infection "Pleurodesis" rates [redacted] 55%

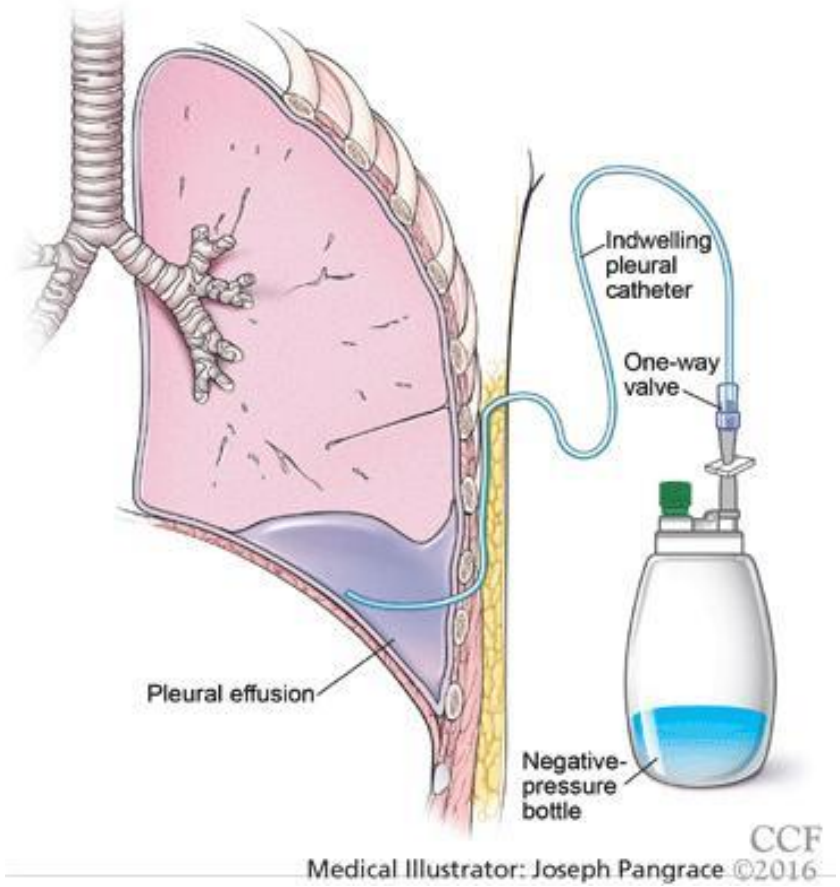
Pleurodesis

- Obliterating pleural space with adhesion of visceral & parietal pleural surfaces by chemically- or mechanically-induced inflammation after removal of the pleural fluid
- Different sclerosing agents all act induce the pleural mesothelial cells to start the cascade of inflammation/fibrosis
- Talc (preferred agent), tetracycline derivatives, bleomycin, doxycycline (pleuritic pain) - Can be associated with ARDS

Malignant Pleural Effusion Pleurodesis

- Prevents recurrence by inducing adhesions between visceral and parietal pleura
- Mechanical or chemical
- Chemical: Talc, doxycycline, D50, other chemical agents
- Talc most commonly used:
  - Slurry through chest tube or poudrage during thoracoscopy
- “Autopleurodesis” occurs in 50-60% of indwelling pleural catheters

Indwelling Pleural Catheter (IPC)







Indications for IPC

Malignant pleural effusion

Chylothorax

Any recurrent symptomatic effusion

Advantages

Ambulatory or bedside

Cost-effective

Symptom palliation

Possible pleurodesis

Reduce repeat procedures

Avoid loculations

Potential issues

Semi-permanent

Infection risk (cellulitis, empyema 2.8%)

Dislodgement

Malfunction

Protein depletion?

Indwelling Pleural Catheter (IPC) Complications & Management

- Patient education is key
- Needs good support
- Drainage daily or QOD
- Close follow up as outpatient
- Auto-pleurodesis 50-60% in 2-4 months

Management Algorithm for Malignant Pleural Effusion (MPE)

Known or suspected malignant pleural effusion
(history of malignancy, cancer risk factors, or suggestive imaging/cytology)

→ **Asymptomatic** → **No pleural intervention needed** (unless for diagnostic purposes)

Symptomatic
(dyspnea, chest discomfort, cough)

Perform therapeutic thoracentesis
- Ultrasound-guided (large-volume tap)
- Send fluid for diagnostic studies (cytology, LDH, protein, etc.)

Improvement in symptoms?
(usually assessed within 24–48 hours)

No improvement

Investigate other causes of dyspnea
- Lung parenchymal disease
- Pulmonary embolism
- Cardiac disease
- Trapped lung (non-expandable lung)
- Others

Symptomatic improvement

Does the lung re-expand after thoracentesis?
(Assess with CXR or ultrasound)

No
(non-expandable lung)

Predicted short survival?
(limited life expectancy, poor performance status)

Yes

Palliate with repeated thoracenteses as needed
± oxygen, opioids for dyspnea

No

Consider indwelling pleural catheter (IPC)
- Also consider in symptomatic loculated effusions or failed pleurodesis
- Allows outpatient management

Yes
(expandable lung)

Discuss options: IPC vs. pleurodesis vs. combination approach
- Patient preference and goals of care
- Life expectancy
- Performance status
- Cancer type and response to systemic therapy
- Local expertise and resources

Talc pleurodesis or talc slurry ± IPC
- For patients with expandable lung and reasonable life expectancy
- Can be done via chest tube or during thoracoscopy

Monitor for IPC-related infection
- Cellulitis, tunnel infection
- Pleural space infection (empyema)

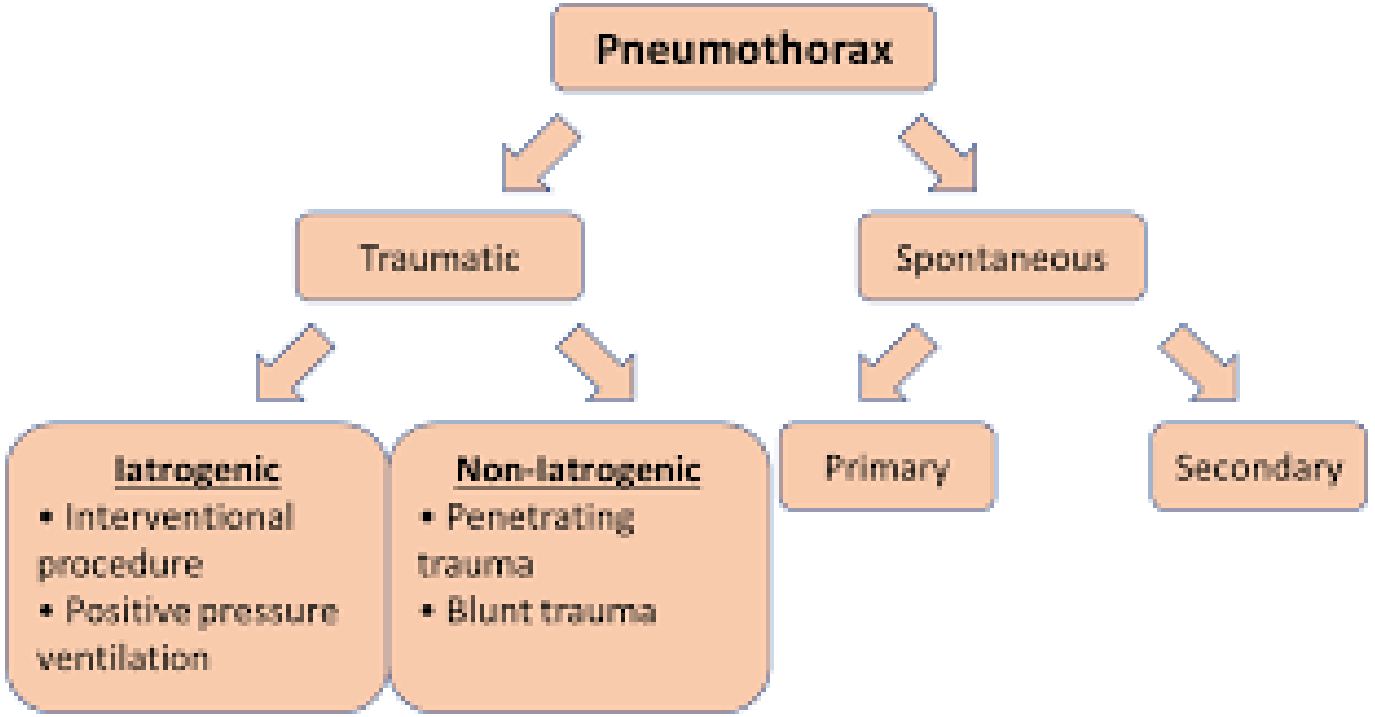
If IPC infection suspected
- Initiate oral antibiotics based on local sensitivities
- Attempt to keep catheter in place (in most cases)
- Remove IPC if persistent infection, sepsis, or lack of response

Abbreviations: IPC = indwelling pleural catheter; MPE = malignant pleural effusion; CXR = chest X-ray
Note: Management should be individualized based on patient symptoms, prognosis, cancer type and response to therapy, and institutional expertise.
This algorithm is a general guide and should be used in the context of current guidelines (e.g., BTS, ACCP, ATS/ERS) and clinical judgment.

Pneumothorax

Pneumothorax (PTX) Definition

- Accumulation of air within pleural space



Primary Spontaneous Pneumothorax (PSP)

- Incidence:
  - 7-18 per 100,000/yr (male)
  - 1- 6 per 100,000/yr (female)
- Risk factors:
  - Male
  - Smoking (cigarette, cannabis)
  - Genetic predisposition
  - Thoracic Endometriosis
  - Birt-Hogg-Dube syndrome

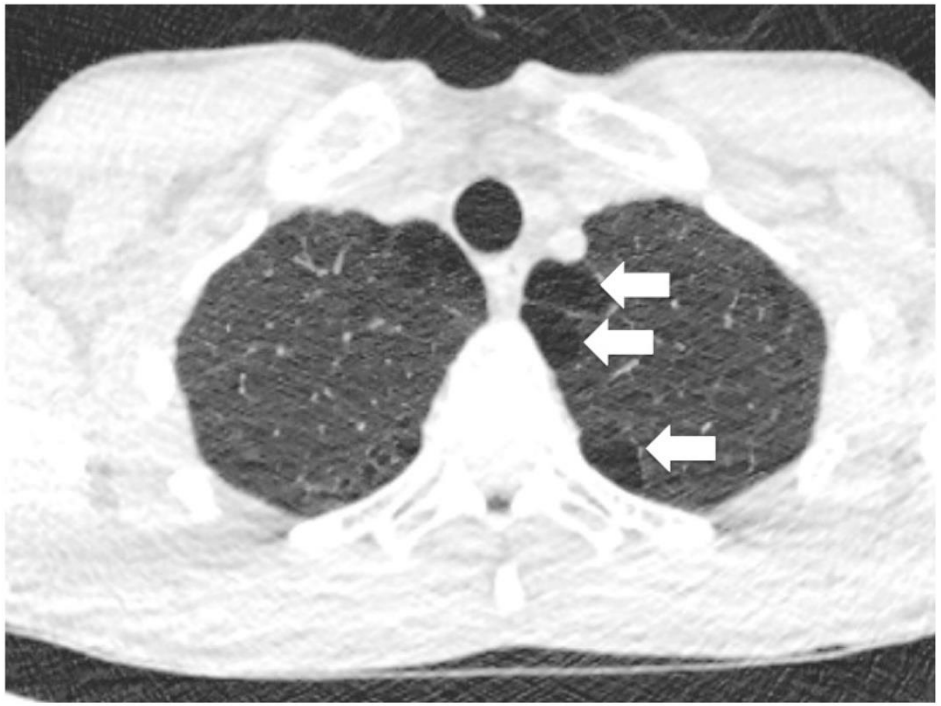
Clinical presentation

- Typically occurs at rest
- Sudden ipsilateral chest pain
- Hypoxemia not uncommon
- Decreased chest excursion
- Diminished breath sounds
- Hyper resonant percussion
- Decreased or absent tactile fremitus

Primary Spontaneous Pneumothorax (PSP)
Etiology

- Exact pathogenesis unclear
- Suspect rupture of subpleural bleb or bulla





Secondary Spontaneous Pneumothorax (SSP)

- Underlying lung dysfunction:
  - COPD
  - Emphysema
  - CF
  - Asthma
  - Infections
  - ILDs
  - Thoracic endometriosis

TABLE 2. CAUSES OF SECONDARY SPONTANEOUS PNEUMOTHORAX.*

Airway disease
Chronic obstructive pulmonary disease
Cystic fibrosis
Status asthmaticus
Infectious lung disease
Pneumocystis carinii pneumonia
Necrotizing pneumonias (caused by anaerobic, gram-negative bacteria or staphylococcus)
Interstitial lung disease
Sarcoidosis
Idiopathic pulmonary fibrosis
Langerhans'-cell granulomatosis
Lymphangioleiomyomatosis
Tuberous sclerosis
Connective-tissue disease
Rheumatoid arthritis (causes pyopneumothorax)
Ankylosing spondylitis
Polymyositis and dermatomyositis
Scleroderma
Marfan's syndrome
Ehlers–Danlos syndrome
Cancer
Sarcoma
Lung cancer
Thoracic endometriosis (related to menses; causes catamenial pneumothorax)

*Categories and disorders are listed according to frequency of occurrence.

Secondary Spontaneous Pneumothorax (SSP)

Clinical presentation

- Symptoms usually more severe than PSP due to underlying disease
- Severity variable
  - Volume of air in pleural space
  - Rapidity of onset
  - Age
  - Respiratory reserve

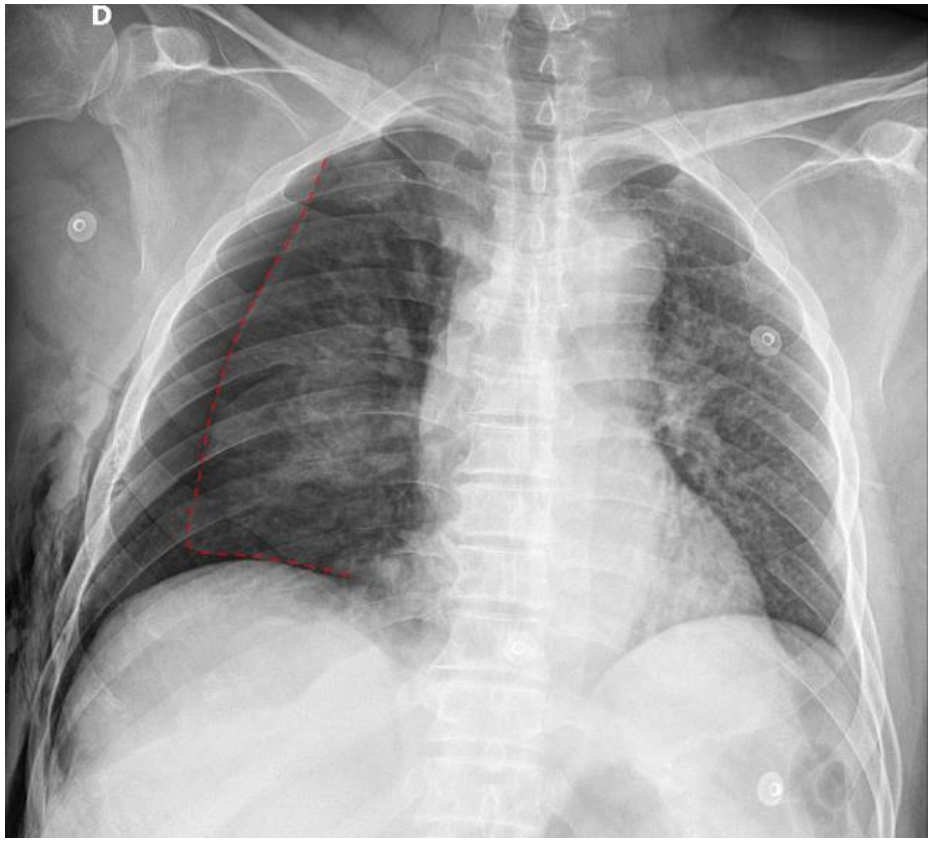
Management:

- Often requires drainage

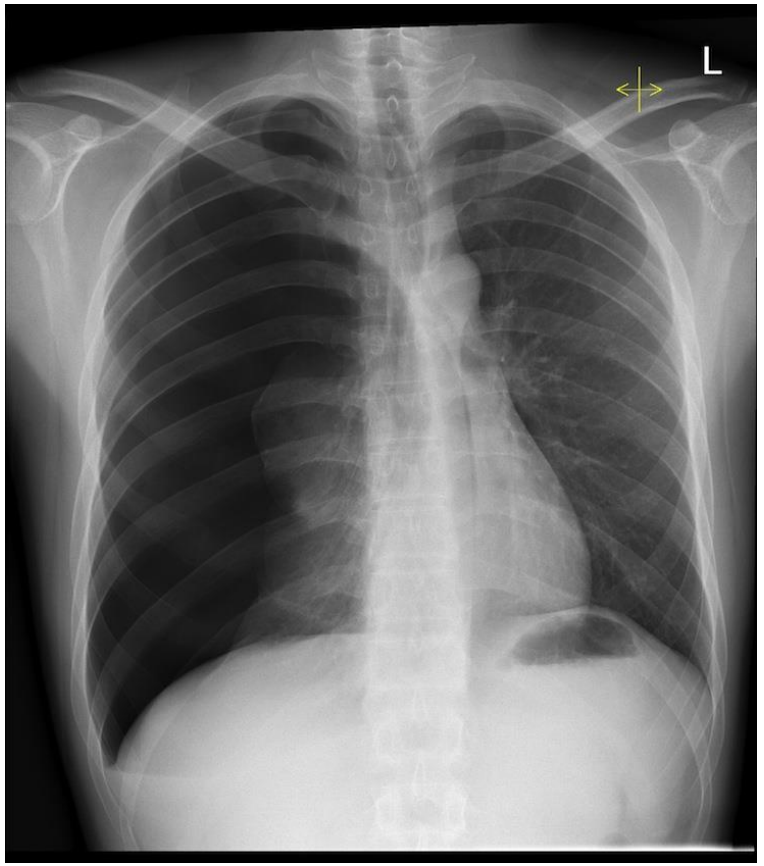
Recurrence:

- Up to 80%
- Often requires recurrence prevention

Imaging of PTX

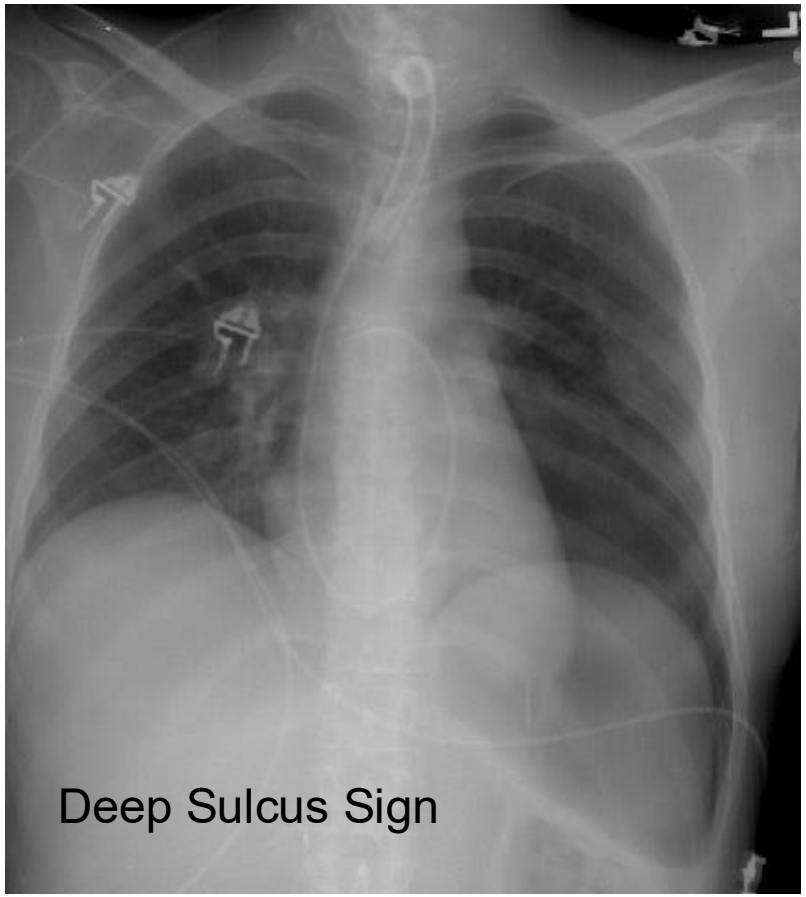


Pleural separation/pleural line
Increased lucency/absence of lung markings

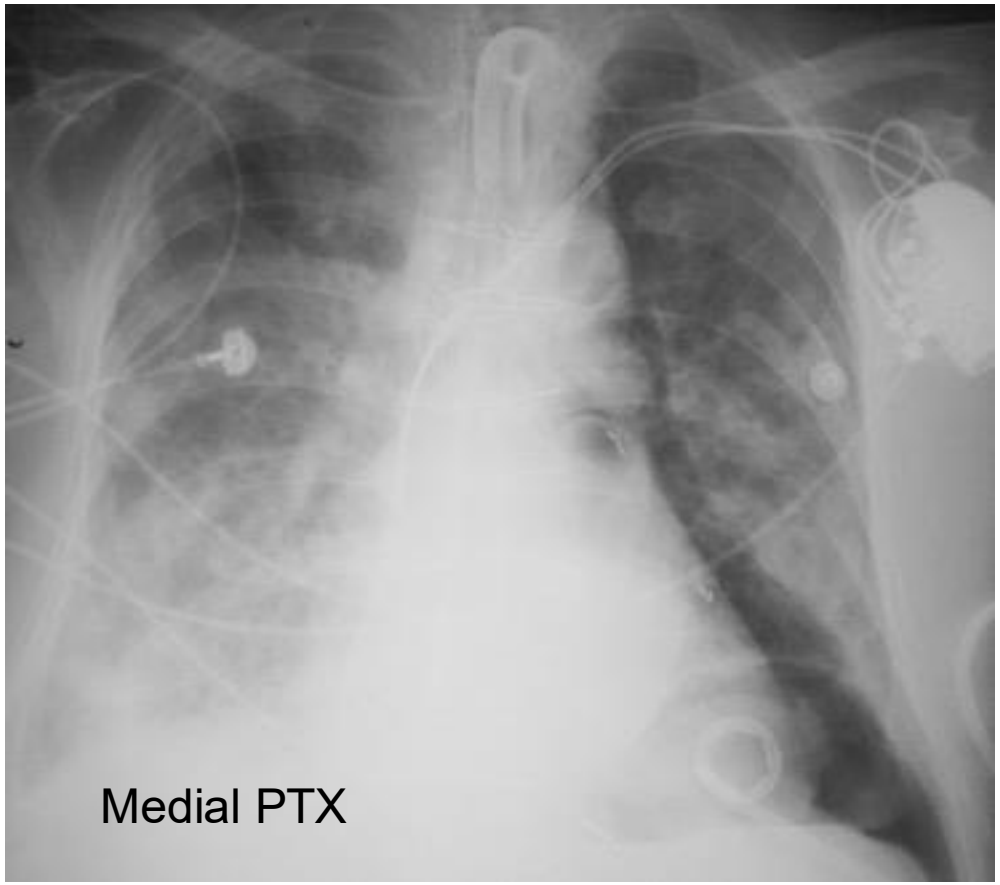


Tension pneumothorax
Radiographic and clinical diagnosis

Imaging of PTX

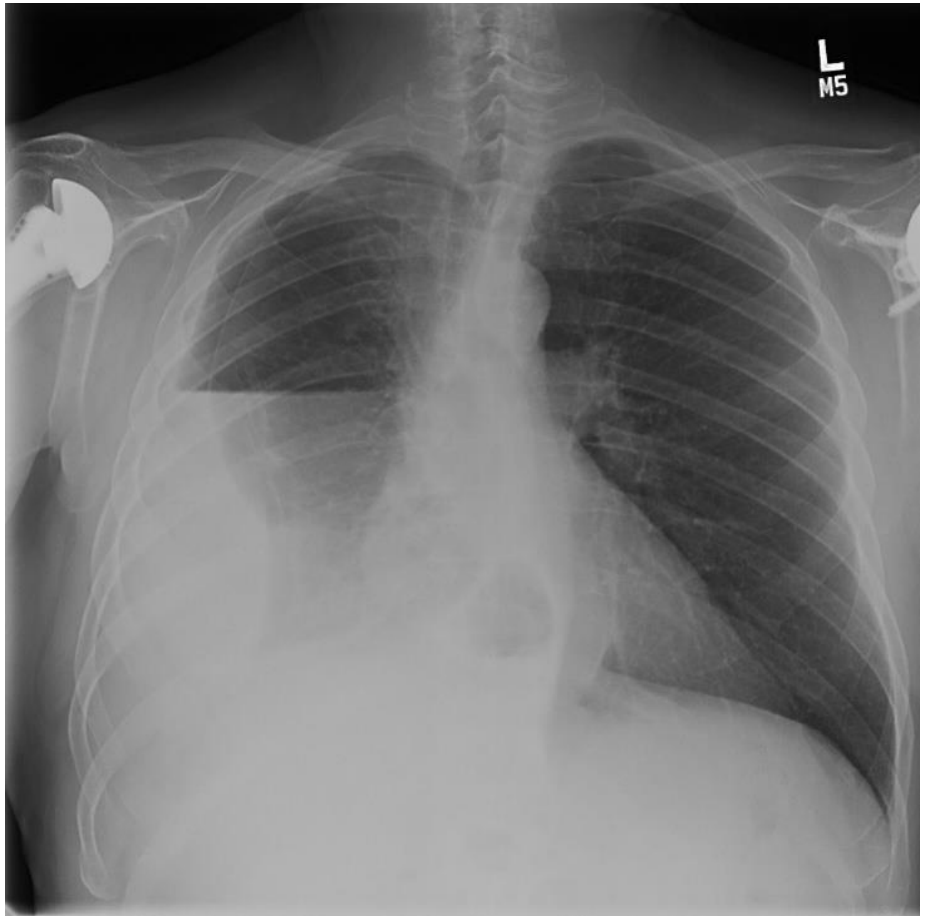


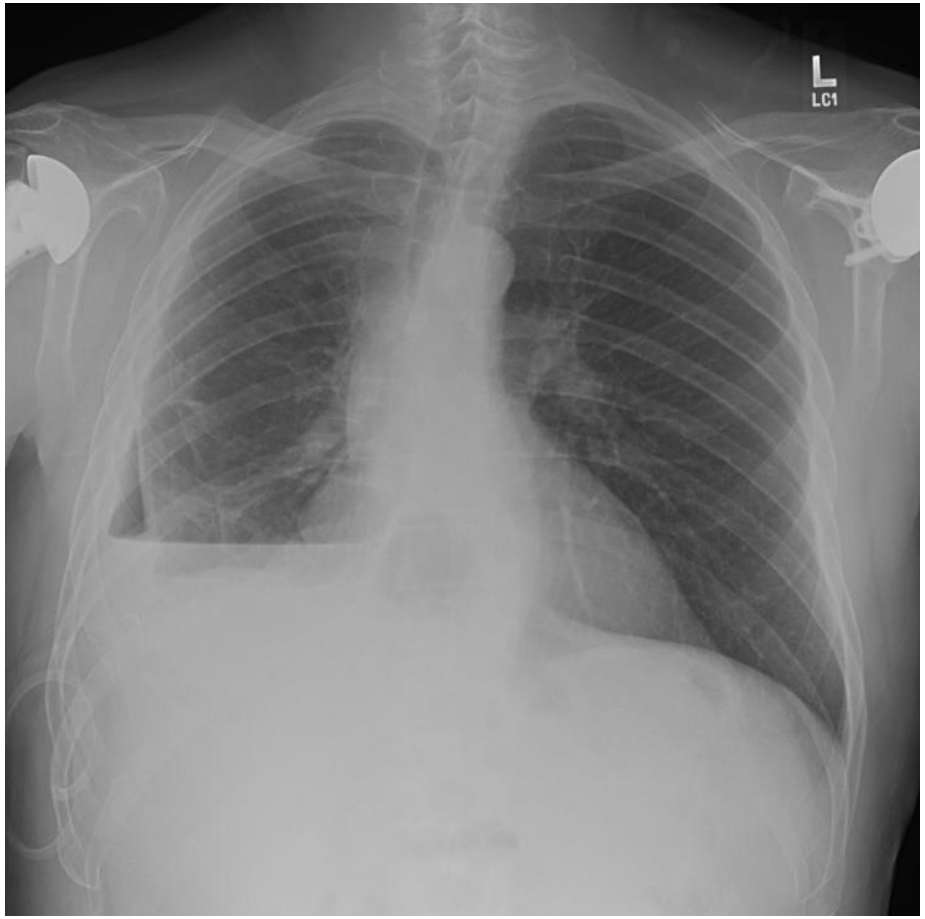
Deep Sulcus Sign



Medial PTX

Hydropneumothorax

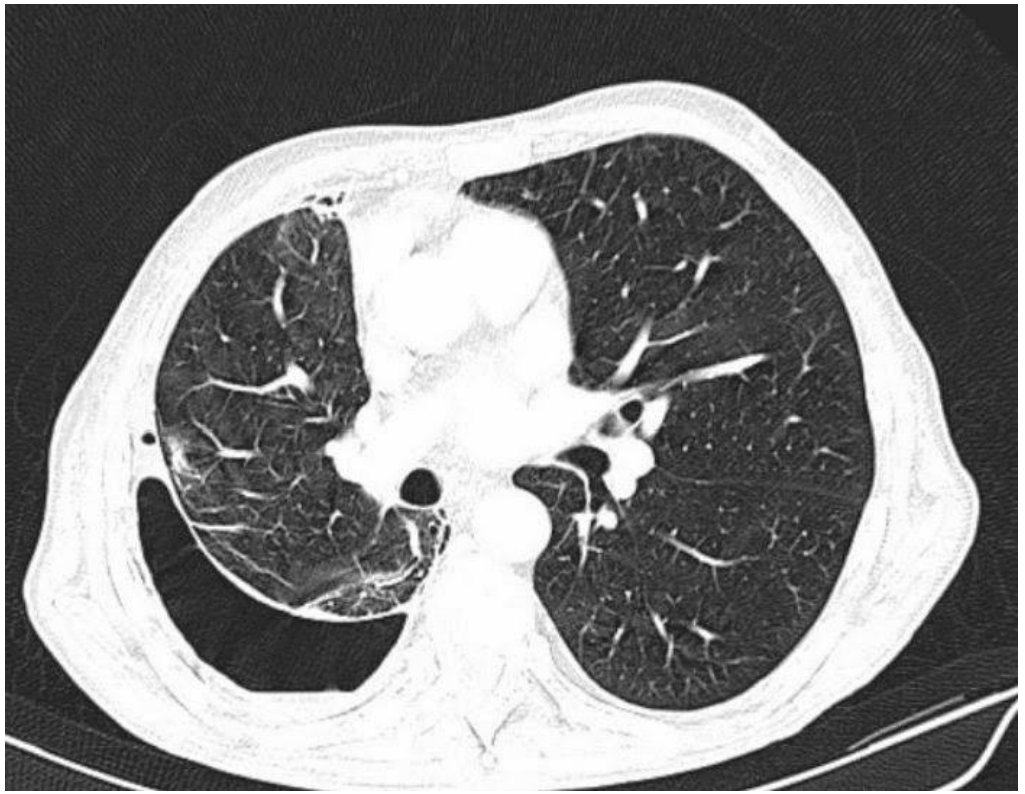




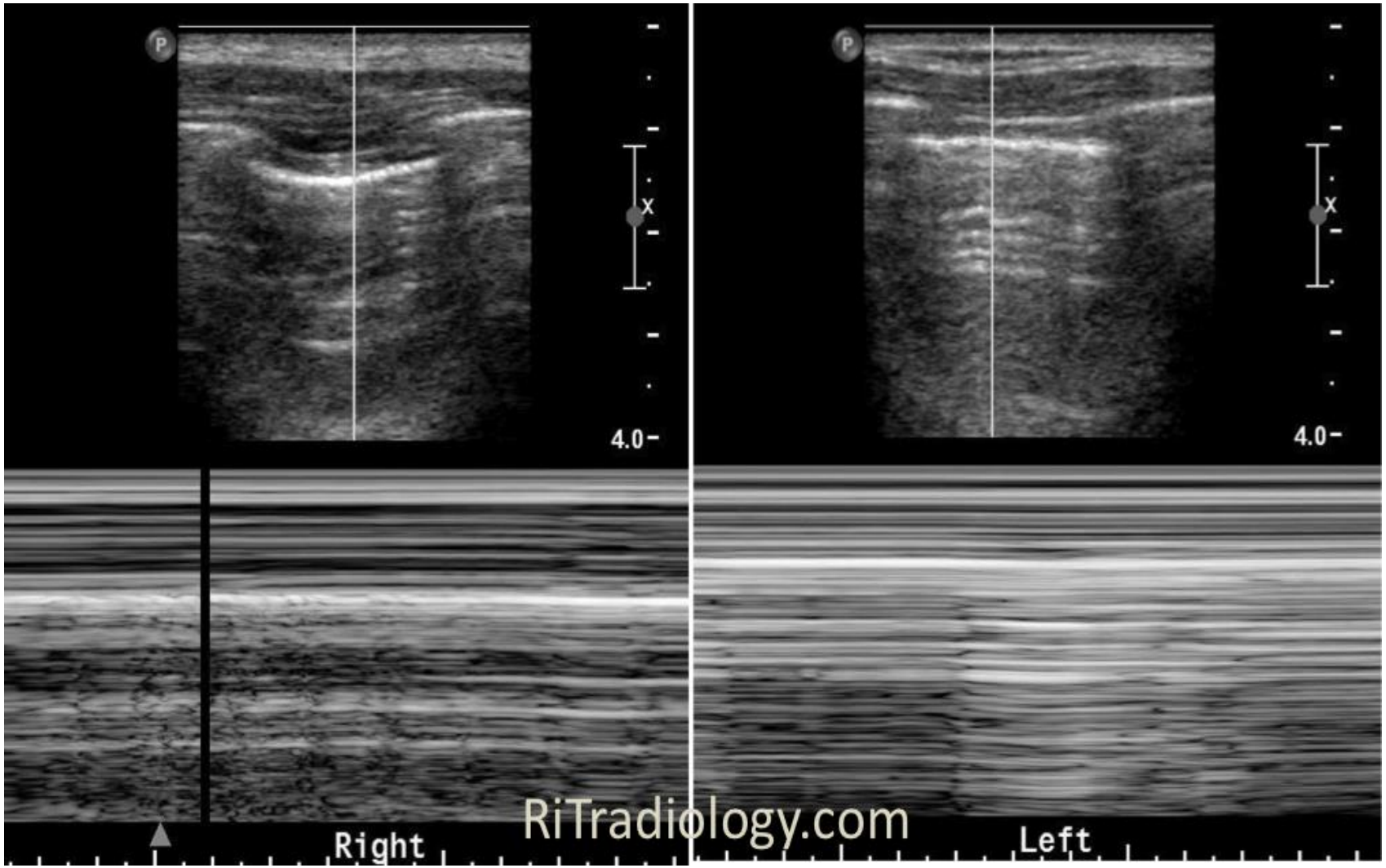
Seen in trauma and in trapped lung after drainage (pneumothorax ex vacuo)

Pneumothorax ex vacuo

- Occurs after thoracentesis when the lung does not expand to fully fill the pleural space.
- Not caused by puncture of the visceral pleura and underlying lung.
- Does not require intervention (often)



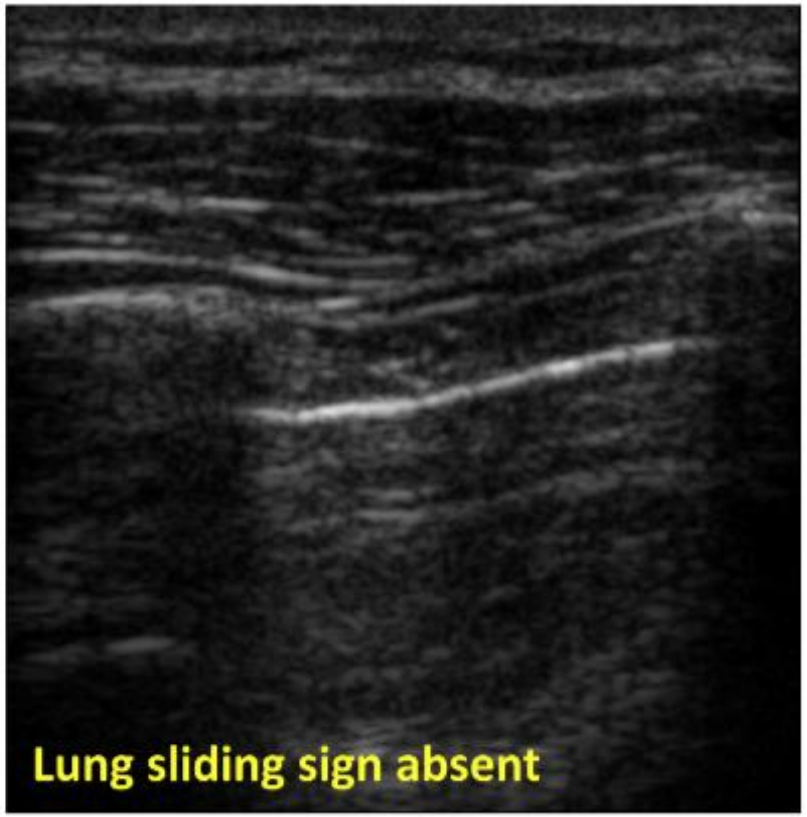
Ultrasound in PTX



- **Stratosphere or barcode sign** (absence of seashore sign)
- Using the M mode on POCUS

Ultrasound in PTX





- **Lung sliding** rules out PTX (NPV approx. 100%)
- Absence of lung sliding not always PTX:
  - emphysema
  - mainstem intubation

- Limitations of US:
- Obesity
- Edema
- Musculature
- SQ emphysema

Pneumothorax Management
Principles and options

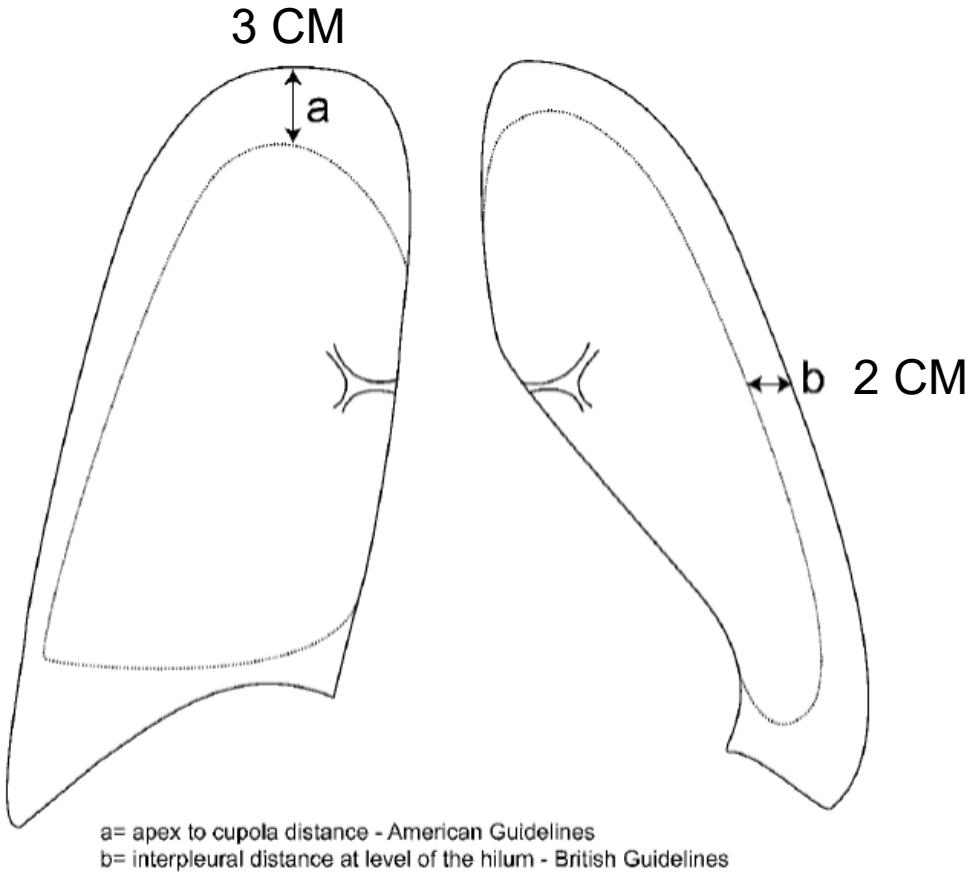
Depends on:

- Stability
- Size
- First or recurrent
- Primary or secondary

Pneumothorax Management Principles (ACCP)

- Degree of clinical compromise >> size of pneumothorax

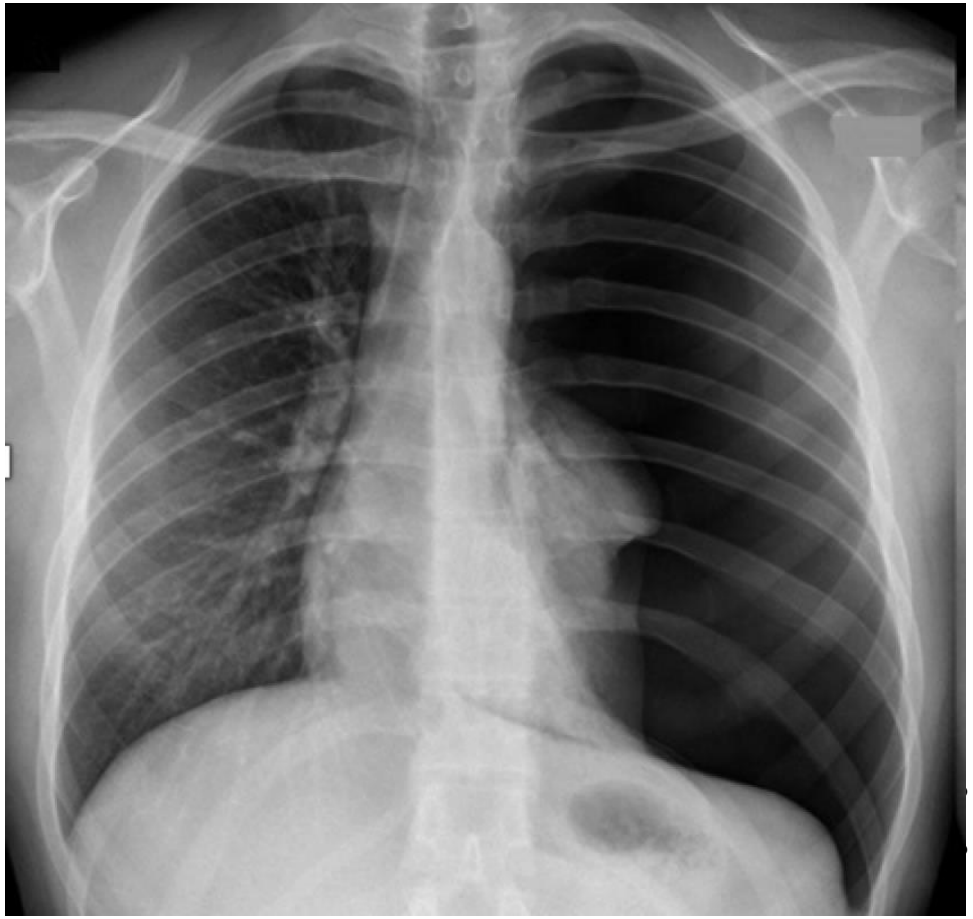
- Stable patients:
- RR < 24
- HR < 120 and > 60 bpm
- RA SPO2 > 90%
- Ability to speak in whole sentences
- Normal blood pressure



a= apex to cupola distance - American Guidelines
b= interpleural distance at level of the hilum - British Guidelines

Figure 1 Depth of pneumothorax.

Tension Pneumothorax

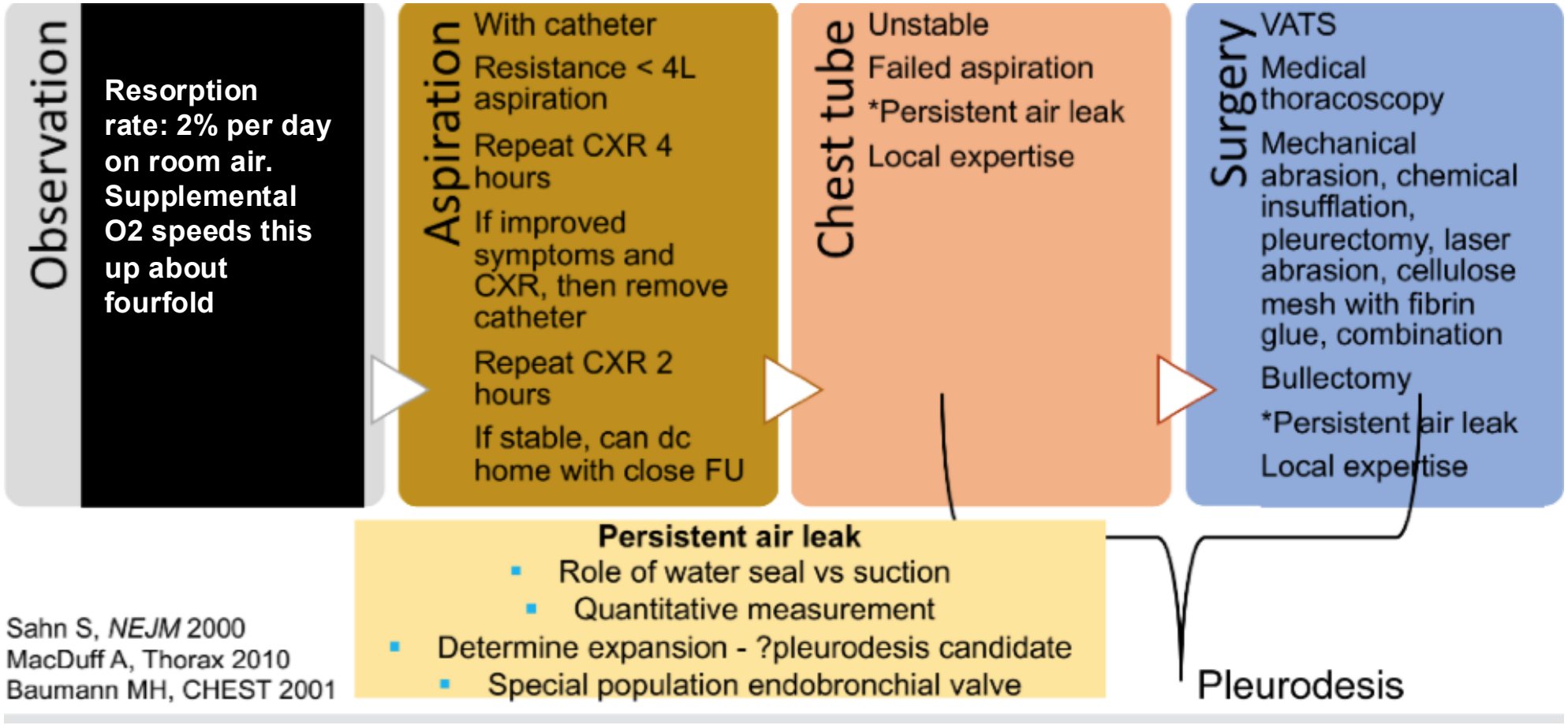


Box 1 Typical clinical situations where tension pneumothorax arises

1. Ventilated patients on ICU.
2. Trauma patients.
3. Resuscitation patients (CPR).
4. Lung disease, especially acute presentations of asthma and chronic obstructive pulmonary disease.
5. Blocked, clamped or displaced chest drains.
6. Patients receiving non-invasive ventilation (NIV).
7. Miscellaneous group, for example patients undergoing hyperbaric oxygen treatment.

EMERGENT treatment with needle decompression
Once stable, place chest tube

Pneumothorax Treatment Options



Sahn S, *NEJM* 2000
MacDuff A, Thorax 2010
Baumann MH, CHEST 2001

PSP Management

- Can be treated conservatively if small and stable
  - Observe clinically +/- CXR at least 4 hours, then in 12 and 24 hours

- Average rate of recurrence 30%
  - Most often in 30 days, but range 6 months to 2 years
  - CT evidence of bullae does not predict recurrence
  - Recurrence prevention often not indicated after 1st occurrence

PSP Management — Key Evidence

RANDOMIZED CONTROLLED TRIALS

Brown et al. | NEJM 2020	Conservative vs. interventional treatment
Hallifax et al. (RAMPP) | Lancet 2020	Ambulatory vs. standard care
Marx et al. | AJRCCM 2023	Needle aspiration vs. chest drain
Chen et al. | Lancet 2013	Minocycline pleurodesis to prevent recurrence

SYSTEMATIC REVIEWS & META-ANALYSES

Mohamed et al. | J Thorac Dis 2024	Needle aspiration vs. chest tube
Cheng et al. | Am J Emerg Med 2024	Aspiration vs. intercostal drainage

Pneumothorax Management Guidelines

- **ACCP 2001: Delphi consensus statement**
- **ERS/EACTS/ESTS 2024 joint guideline**
- **BTS 2023**

ACCP 2001 Delphi consensus statement (Updated guidelines expected 2026)

- **Stable, small PSP:**
  - Observe 3–6 hrs, Discharge if repeat X-ray with no progression, with follow-up in 12 h–2 days.
  - Aspiration or a chest tube if pneumothorax enlarges.
- **Stable, large PSP:**
  - Aspiration or chest tube + Admit in most cases.
  - Reliable patients may go home on a Heimlich valve with follow-up within 2 days.
- **Unstable, large PSP:**
  - Admit and place a 16–22F tube.
  - Use 24–28F if a large air leak and/or positive-pressure ventilation.
  - Add suction if the lung does not re-expand on water seal
- **Simple aspiration:** "rarely appropriate in any clinical circumstance."

ERS/EACTS/ESTS 2024 (joint GRADE guideline)

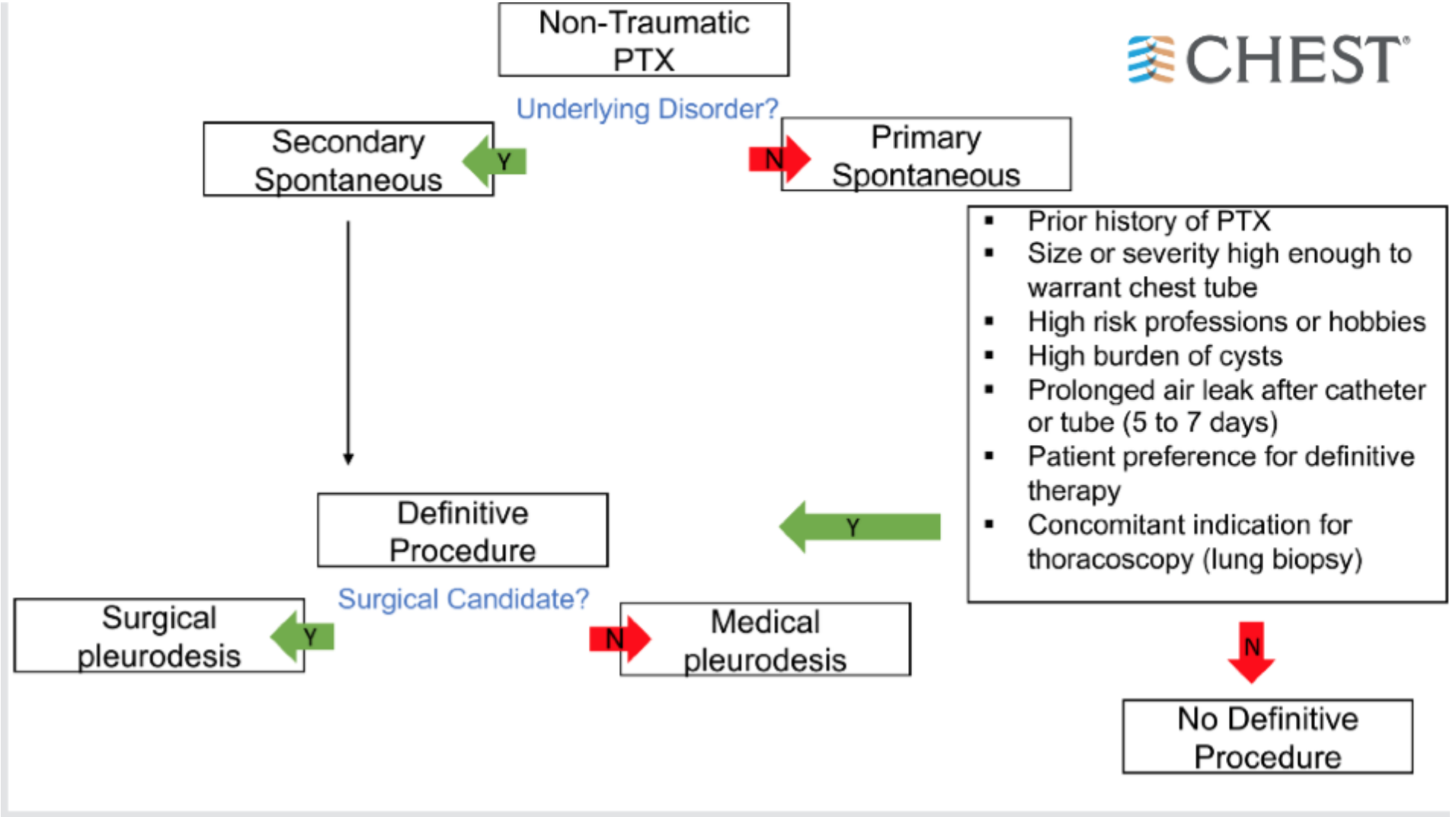
- **Conservative care** for minimally symptomatic, clinically stable PSP
- **Needle aspiration over a chest drain**
- **Ambulatory management:** conditional recommendation

BTS 2023 (British Thoracic Society)

- **PSP**
  - Small (<2 cm) and no significant dyspnea: Observation and possible discharge
  - Large (≥2 cm) or symptomatic: Needle aspiration first
  - Failed aspiration: Chest tube drainage.
- **SSP**
  - Small (less than 1 cm): Hospital admission and observation.
  - Moderate (1-
    2 cm), without significant dyspnea: Consider needle aspiration and inpatient observati
    on.
  - Large (≥2 cm) or significant dyspnea: Chest tube drainage

- **Chest tubes**: Small-bore drains (10–
  14 Fr) generally preferred; routine suction not recommended.

PTX recurrence prevention

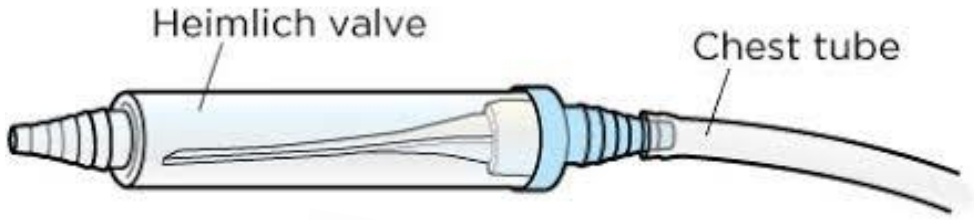


Pneumothorax
Persistent air leak

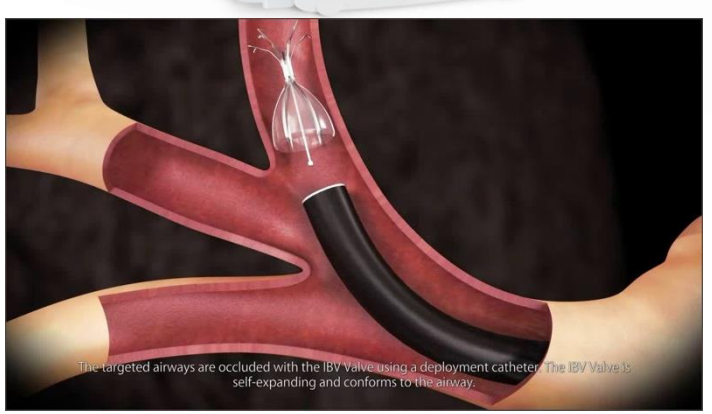
- Air leak > 5-7 days
- More common in SSP and trauma
- Alveolar-pleural fistula or Bronchopleural fistula
- Severity:
  - Grade 1 - forced expiration only
  - Grade 2 - passive expiration only
  - Grade 3 – inspiratory cycle only
  - Grade 4 – inspiration and expiration

Persistent air leak Management

- Outpatient Chest tube with Heimlich valve or automatic water seal
- Surgical repair (VATS/wedge resection with pleurodesis, mesh, flap)
- Blood patch
- Pleurodesis through chest tube
- Bronchoscopic approach: valves, spigots







Questions?