Pleural Disease

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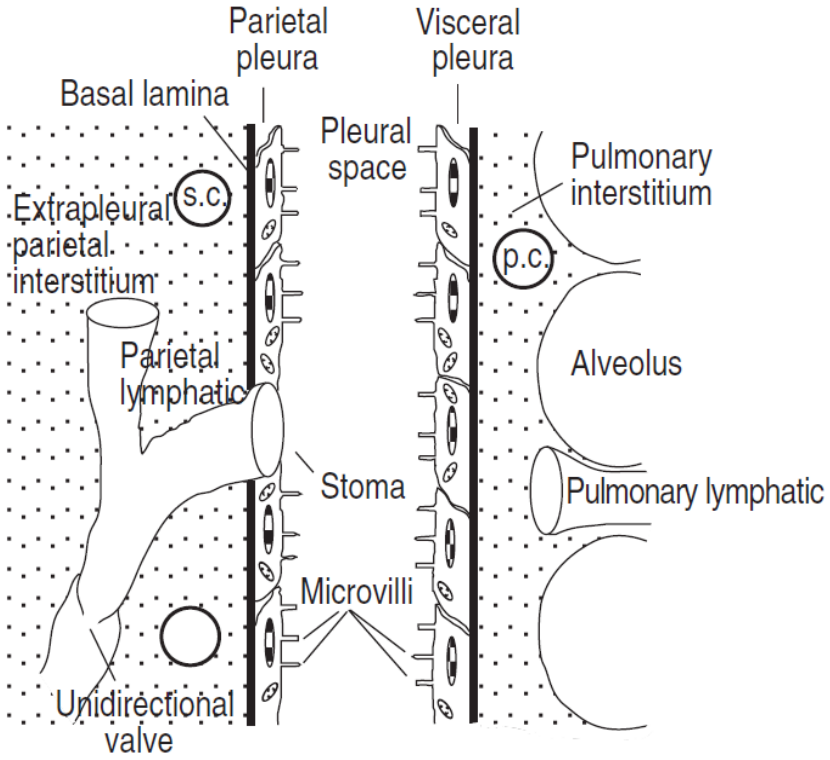
Pleural physiology



- Pleural fluids ~0.3cc/kg
- Produced by mesothelial cell
- Production at the upper part of the pleura and absorption at the diaphragmatic and mediastinal surfaces of the pleura
- The flow rate can increase to pleural fluid filtration
- 10% increase in flow , pleural fluid increase by 15%

Question

Which of the following statements is not correct in regards to pleural physiology?

A. Approximately 0.3ml/kg body mass of pleural fluid is normally in the pleural space

B. Lymphatics course through the visceral pleura to drain the pleural space

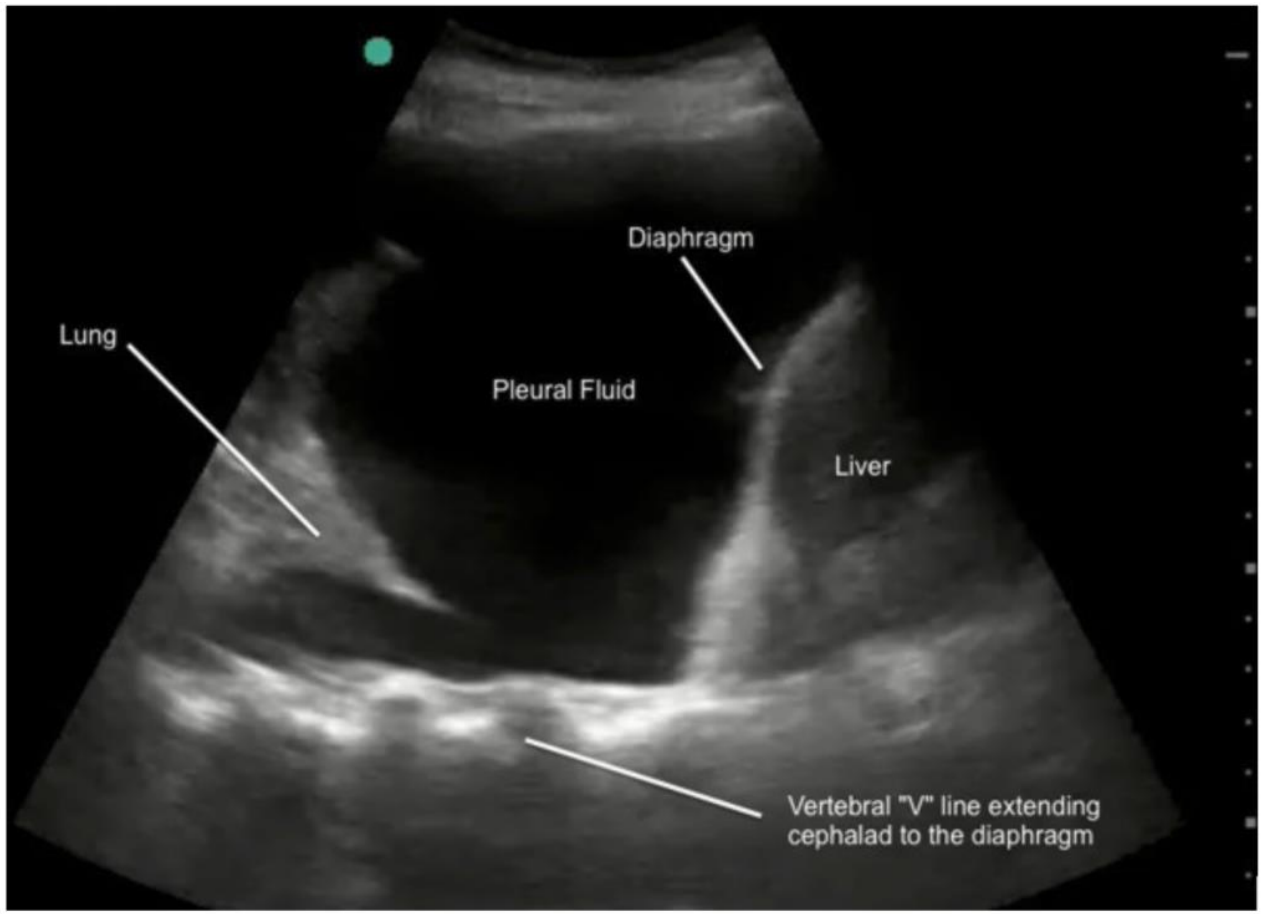
C. Alveolar pressure = atmospheric pressure when lungs expanded

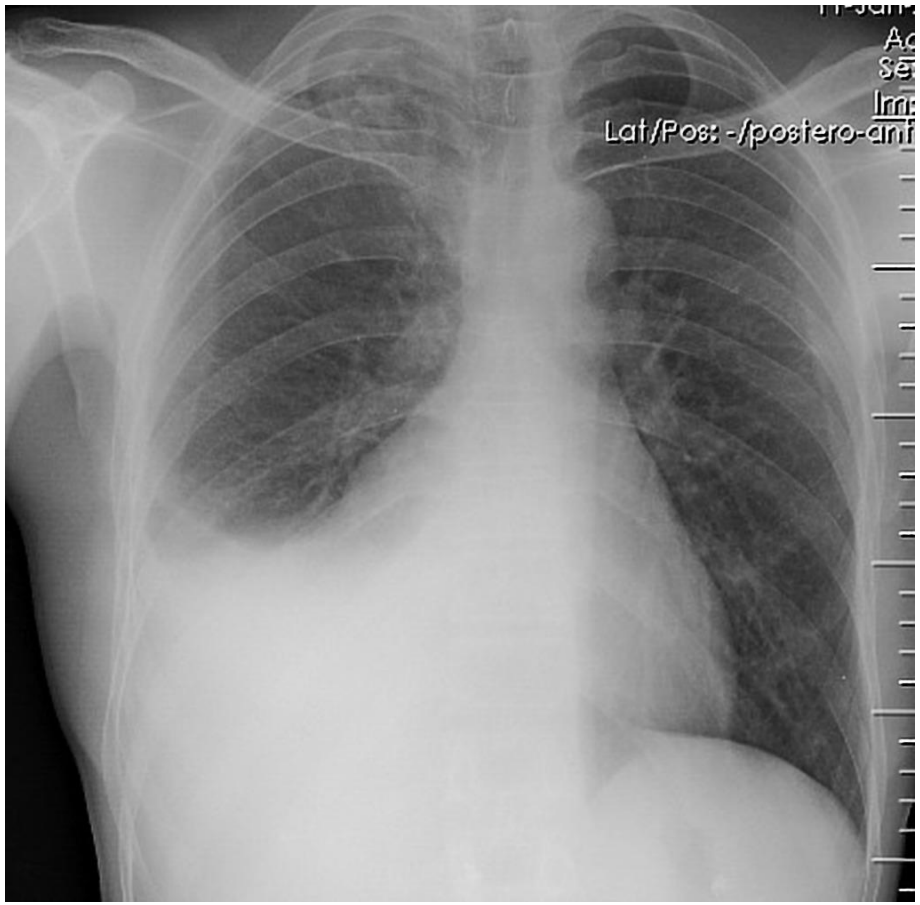
D. Pleural lymphatic flow mostly localized to diaphragm & mediastinal surfaces

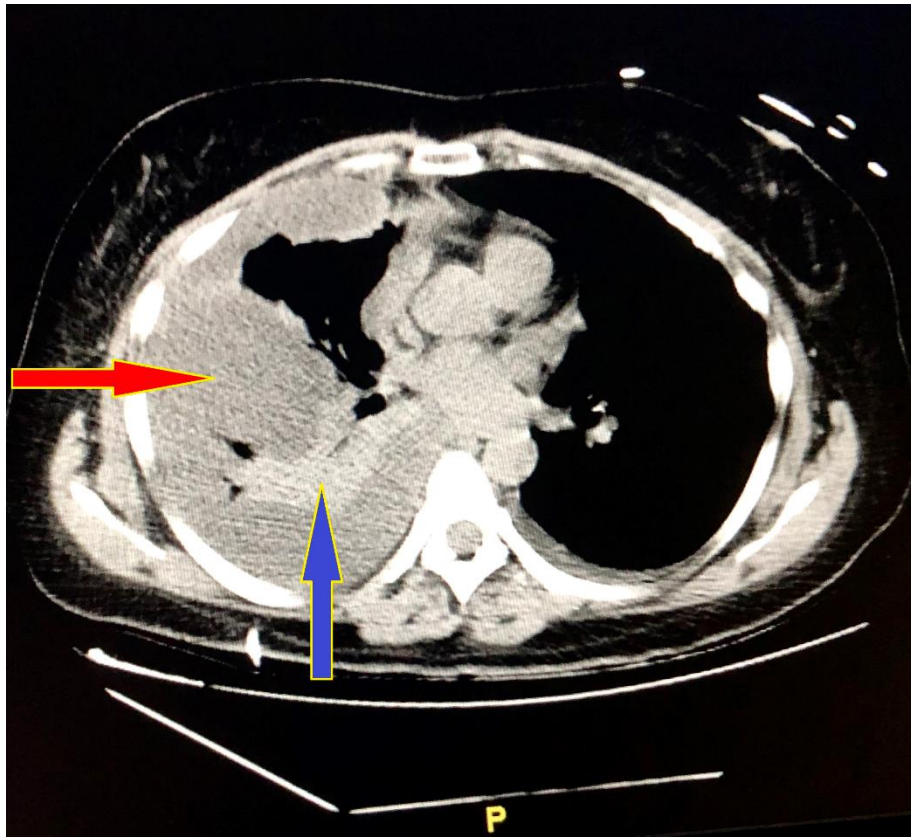
Ans: C

Pleural diagnostics

- Chest x ray can detect pleural fluid once more than 250 cc (Done as the initial invx)
- Lower volumes can be detected in lateral decubitus
- Lung US can detected very small amount of pleural fluids ↳ Main invx
- CT chest with contrast is useful to help plan for surgery , look for pleural thickening


Diaphragm
Lung
Pleural Fluid
Liver
Vertebral "V" line extending
cephalad to the diaphragm


Lat/Pos: -/postero-ant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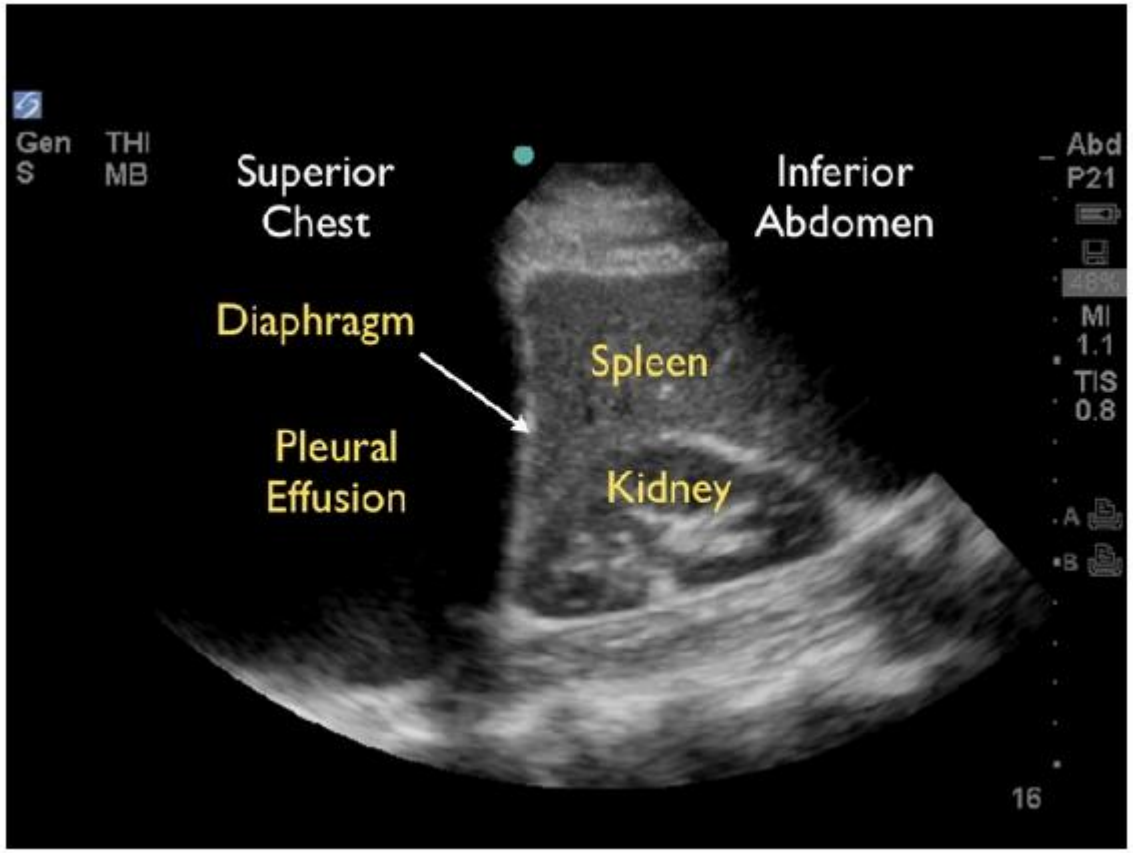

Gen
S
THI
MB
Superior
Chest
Inferior
Abdomen
Diaphragm
Spleen
Pleural
Effusion
Kidney
Abd
P21
MI
1.1
TIS
0.8
A
B
16

Mechanism of pleural collection

- Pleural injury – increased pleural membrane permeability & protein-rich exudates
- Increased intravascular hydrostatic forces and/or decreased oncotic forces that cause protein-poor transudates
- Extravasation of fluid from lymphatic or vascular structures or from an adjacent body compartment into pleural space
- Pleural fluids may accumulate in systemic disease like Rheumatoid arthritis , SLE
- Local disease like pneumonia
- Disease of specific organ system like CHF, liver failure, pancreatitis

* We don't do thoracocentesis in a pt w/ clear cause (eg: pt came w/ CHF & pleural effusion).

WHEN WE DO THORACENTESIS ?

(1) Empyema (infx)

(2) Hemothorax (risks for infx & calcification)

(3) Malignancy (in a pt who is not known to have malignancy)

(4) Symptomatic pt

Pleural Fluid analysis

- First step is to determine transudate versus exudate
  - Pleural fluid/serum protein ratio indication of capillary permeability
  - Pleural fluid/serum LDH ratio indication of inflammation in pleural space

Light's Criteria:

Any one of:

1. Pleural fluid/serum protein ratio > 0.5
2. Pleural fluid/serum LDH ratio > 0.6
3. Pleural fluid LDH > 2/3 upper limit of normal serum LDH

❖Any of the above meets the criteria of exudate

❖Falsely classify about 25% of transudates as exudates usually related to diuretics

Other tests

- Glucose → eg., inflam, infx, malignancy (↓ Glucose)
- Cholesterol → To diff btw transudate & exudate
- Triglyceride (>110 mg/dl) → To dx Chylothorax (>110 confirms) + Milky like color
- Lipase & amylase → If suspected Pancreatic Pleural effusion ↓ Usually on the LEFT SIDE
- Cytology ⇒ Always sent to dx occult Malignancy
- Gram stain and cultures
- Cell count and differential V. imp.
  - ↳ to dx inflam
    - → Neutrophils (parapneumatic effusion)
    - → lymphocytes (Malignancies, chylothorax, lymphomas, some syndromes)
    - → Eosinophils (esophageal rupture, ..)

Etiology of Pleural effusion

Causes of pleural fluid transudates and exudates.

Transudates	Exudates
Heart failure (> 90% of cases)	Pneumonia (parapneumonic effusion)
Cirrhosis with ascites	Cancer
Nephrotic syndrome	Pulmonary embolism
Peritoneal dialysis	Bacterial infection
Myxedema	Tuberculosis
Atelectasis (acute)	Connective tissue disease
Constrictive pericarditis	Viral infection
Superior vena cava obstruction	Fungal infection
Pulmonary embolism	Rickettsial infection
	Parasitic infection
	Asbestos
	Meigs syndrome
	Pancreatic disease
	Uremia
	Chronic atelectasis
	Trapped lung
	Chylothorax
	Sarcoidosis
	Drug reaction → eg: Drug-induced lupus drug (HYDRALAZINE, isoniazid, & procainamide). ← MAINLY.
	Post–myocardial injury syndrome

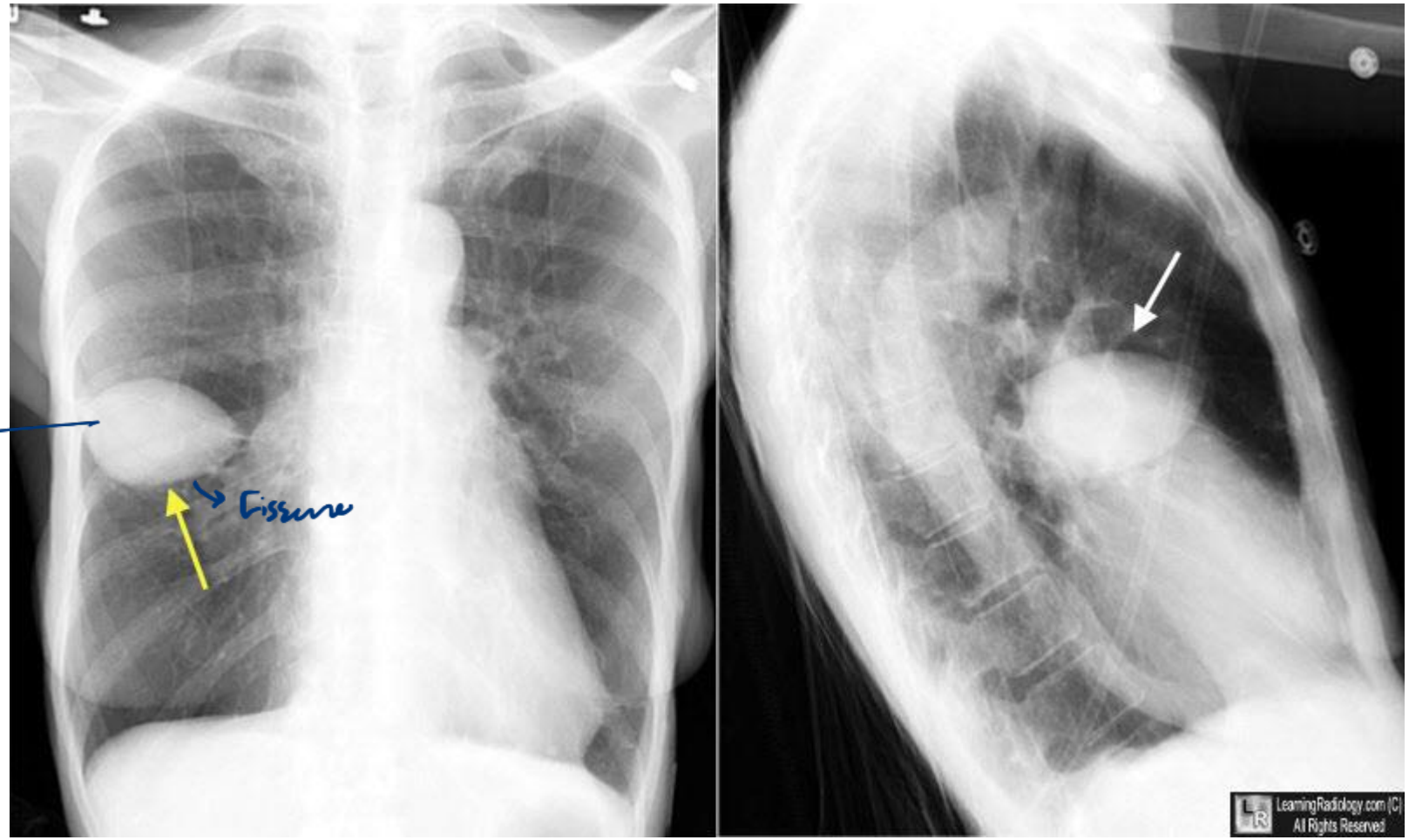
Everything else

Source : Current Medical Diagnosis and Treatment 2018

Transudative Pleural effusion

- Congestive heart failure most common; usually bilateral
- Hepatic hydrothorax – liver cirrhosis & portal hypertension without cardiac or pulmonary pathology → Right Sided
- Most commonly right-sided (80%) although can be either
- Ascites traversing from peritoneal to pleural space via diaphragmatic fenestrations & pressure gradient (peritoneal space=high; pleural space=low)
- *Ascites cannot be detected in up to 20%*
- Treatment involves sodium restriction & lowering portal pressures
- Spontaneous infection of hydrothorax (15%)
- PF neutrophil count > 250 cells/uL with +culture or > 500 cells/uL with -cx

Pseudotumor ←
(Fluid collection
btw Rt upper
& Middle lobes



Transudative Pleural effusion

- Nephrotic syndrome – Excessive loss of plasma proteins in urine
- Includes hypoalbuminema, hypercholesterolemia, & peripheral edema

Excretion of total proteins > 3.5g/d

- Urinothorax – Rare complication of obstructive uropathy

Pleural fluid creatinine > serum creatinine; low pH; low glucose

- Renal scintigraphy = tracer flow from urinary tract to pleural space

very common !!

Exudative Pleural effusion

- Malignant pleural effusion - Lung, breast, lymphoma M.C.
- Diagnostic yield of pleural fluid cytology =66% (subsequent taps)
- Tuberculous pleural effusion → Lymphocyte
    - Lymphocyte/neutrophil ratio ≥ 0.75 (>60% lymphocytes)
    - Meta-analysis = yield of adenosine deaminase (ADA) to have sensitivity 92%; specificity 90% -
    - ADA-2 isoform improves yield; stimulated in presence of live organisms
- Pleural Infection – parapneumonic effusions & empyema

VAT (video-assisted thoracoscopy) When: ⇒ If exudative pl. fluid analysis & -ve malignant cells on cytology.

Exudative pleural effusion

- Chylothorax :
    - Turbid, milky – chyle in pleural space from thoracic duct obstruction
    - PF triglyceride > 110 mg/dL(check chylomicrons)
    - Thoracic duct follows path of abdominal aorta; at level of 5th thoracic vertebra duct crosses to left
    - Below level of crossing – right-sided; Above – left-sided
- Yellow Nail Syndrome – deformed yellow nails, lymphedema, effusion ⇒ Recurrent Chylothorax
- Lymphangioleiomyomatosis – women (cysts), mutations in tuberous sclerosis complex-2 gene, angiomyolipomas

↳ In Lungs
↳ (LAM). causes recurrent pleural effusions.
→ formed in the kidneys.

Exudative pleural effusion

- Rheumatoid Arthritis Very sick pt, febrile..
    - Most common intrathoracic manifestation of RA (20%)
    - Typically pH< 7.20; glucose <50mg/dL; pleural/serum glucose ratio <0.5;

      elevated LDH (>1,000 U/L), rheumatoid titer > 1:320
    - Associated with rheumatoid nodules
- Systemic Lupus Erythematosus
    - 30% = pleuritis (independent predictor of mortality); pleural fluid ANA NOT helpful but presence of LE cells is highly specific

→ Poor prognostic sign

↳ Lupus

- Benign Asbestos-Related pleural effusion
    - Most small, asymptomatic, recurrent

Exudative pleural effusion

- Pancreatitis – if chronic ? pancreatic-pleural fistula – high amylase levels (>1000)
- Perforated esophagus – iatrogenic or post-vomiting (Boerhaave Syndrome) - Lt sided, ↓↓ pH
- Usually left-sided; very low pH < 7.00 & high amylase (salivary)
- Meig's Syndrome (Ascites + pl. effusion + benign ovarian tumors)
- Ascites & effusion with benign ovarian tumor (fibroma), increased CA-125, R>L
- Hemothorax – trauma, iatrogenic, catamenial; PF Hct >50% blood Hct
- Pulmonary Embolism
- Vasculitis – Granulomatous Polyangiitis – pleural involvement by necrotizing vasculitis
- Biliothorax – Complication of percutaneous biliary drainage, radiofrequency ablation
- Unusual things – Sarcoid, myxedema, amyloid, extra medullary hematopoiesis, drugs

Rt. sided

↳ fibromas

→ Lt sided pl. effusion bc peripancreatic fluid seeps through the openings of the diaphragm, the panc. tail ends at the hilum of the spleen & it's so close to Lt hemidiaphragm, so pancreatitis in head & body of panc. → we'll NOT see pl. effusion (seen only in whole body & tail inflam.).

Pleural effusion post open heart surgery

- CABG-related effusions
    - Early (within 30 days) – usually bloody; may contain >10% eosinophils
    - Late (> 30 days) – non-bloody, lymphocyte predominant
- Post-cardiac injury syndrome (Dressler's) – ≥1 week myocardial injury
- Pericarditis, pulmonary infiltrates, pleural effusions
    - Chest pain, fever, leukocytosis, pleuropericardial friction rub
    - PF in 60-80%; small, left-sided; hemorrhagic with neutrophil predominant exudate during acute phase evolving to lymphocyte predominant – resolves with anti-inflammatory drug therapy

Tx: NSAIDs.
↳ pleuritis

Pleural fluid due to pneumonia

- **Parapneumonic effusion** = any effusion from pneumonia that happens in 25-57%
- Uncomplicated, Complicated, & Empyema
    - Uncomplicated - generally resolves with antibiotic therapy alone
    - Complicated - requires tube drainage or surgery
    - Empyema (presence of pus or bacteria) - must always be drained
- No organism grown in 40% with pleural infection
- Higher yield if inoculate PF into blood culture bottle at bedside
- Delay in effective pleural drainage may significantly increase
- morbidity
- Complicated effusion might rapidly evolve into complex empyema requiring surgery

SUMMARY OF CHARACTERISTICS FOR PLEURAL INFECTION DIAGNOSIS AND MANAGEMENT

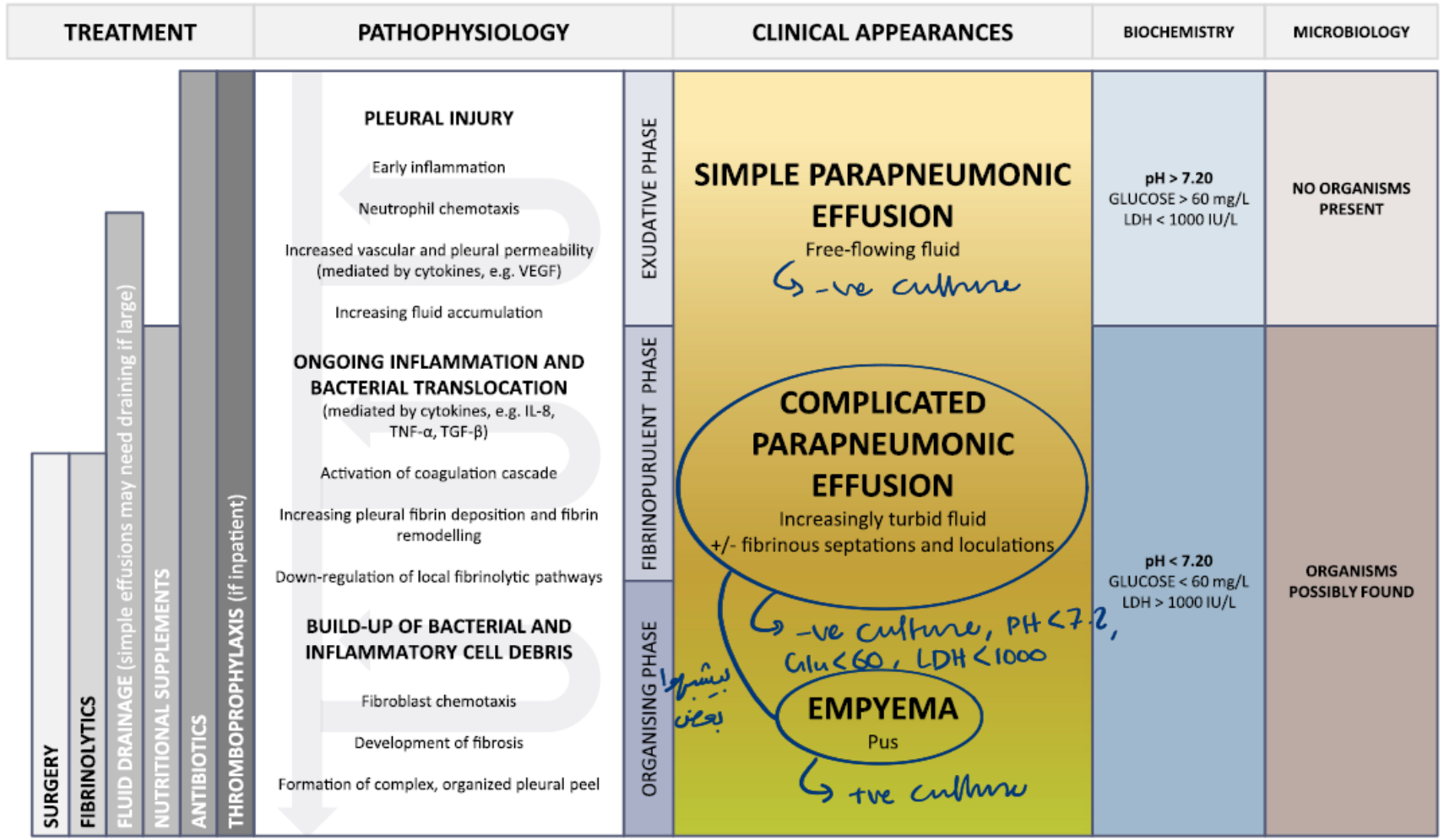


Fig. 2. The pathophysiology, appearance, diagnostic parameters, and treatment options of infected pleural effusions.

COMMUNITY ACQUIRED CAP
85% Strep. & staph

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%		
OTHER 5%		

'Anaerobes' includes Fusobacterium, Bacteroides, Peptostreptococcus , Unclassified mixed anaerobes, *Prevotella* spp., *Clostridium* spp., *Mycobacterium tuberculosis* and *Actinomyces* spp.

HOSPITAL ACQUIRED → Mostly.
15% Staphy & G-ve organisms.

AEROBES 88%	***STAPHYLOCOCCI* 40%**	***MRSA* 71%**
		S. aureus 29%
	GRAM NEGATIVE 26%	
	STREPTOCOCCI 21%	
	ENTEROCOCCCI 13%	
ANAEROBES 8%		
OTHER 4%		

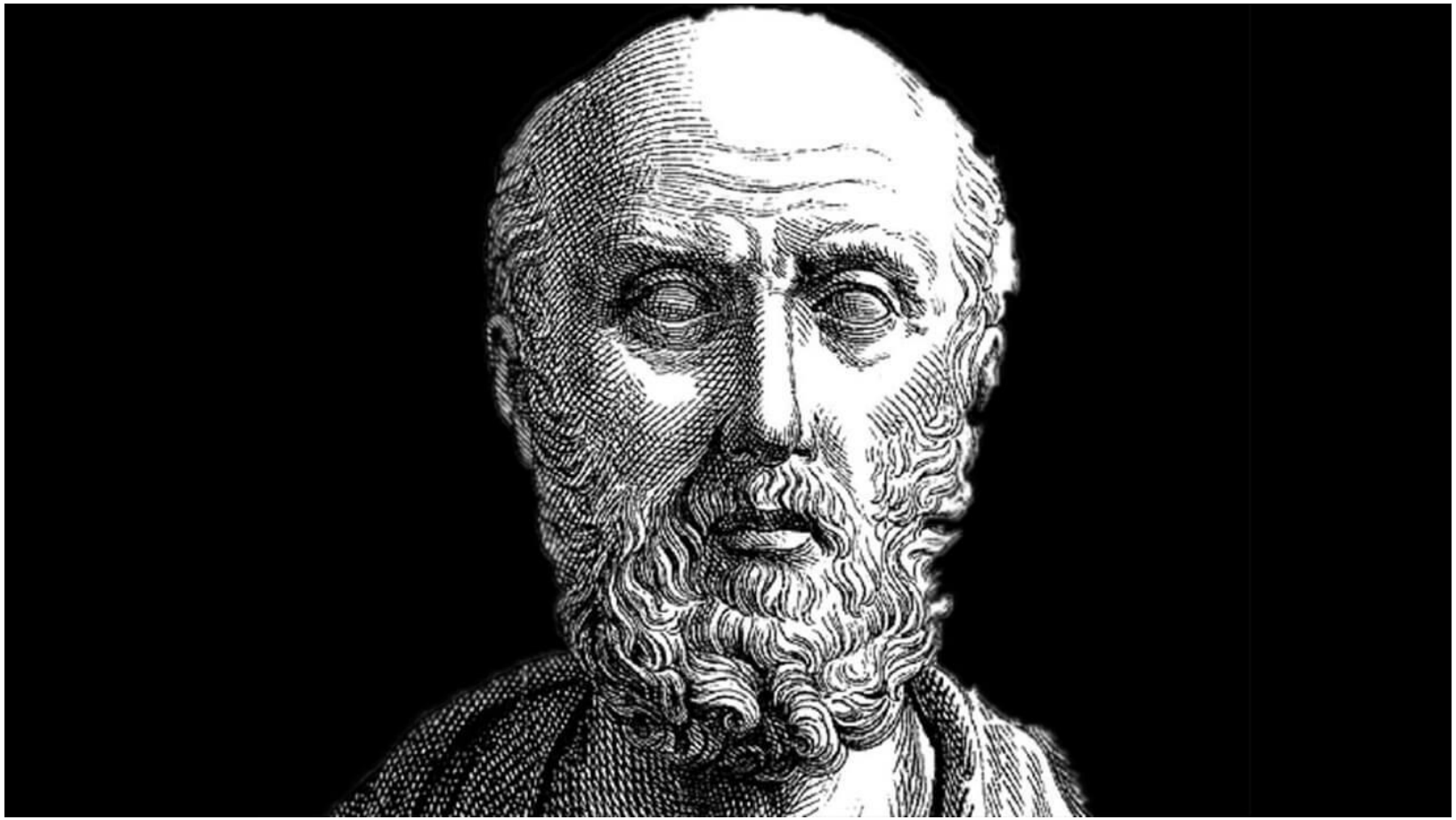
'Gram negative' includes *Escherichia coli,* Other coliforms, Proteus, *Enterobacter* spp. and *Pseudomonas aeringosa*

'Other' includes *Burkholderia anthina*, *Eikenella*, *Haemophilus influenzae*, oral bacterium, *Pasterella multocida*, and *Klebsiella* spp.

Tx of pneumonia ① Abx ② Drain if suspected Paraneumonic eff. or empyema

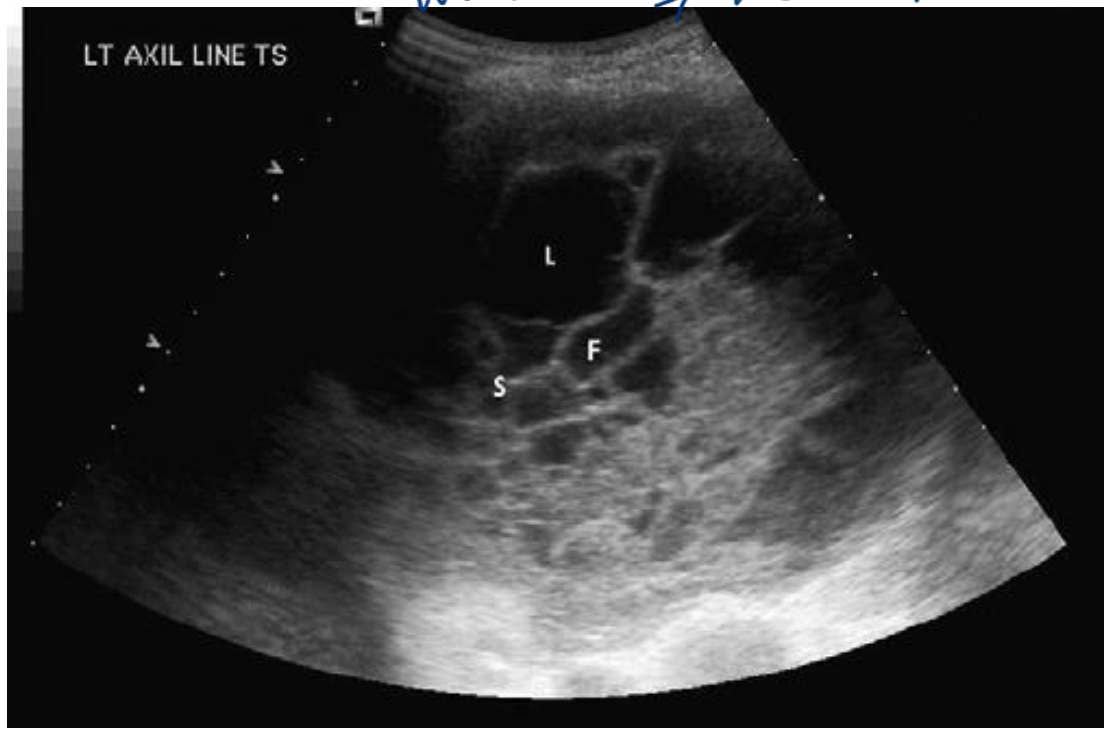
Complicated parapneumonia and empyema

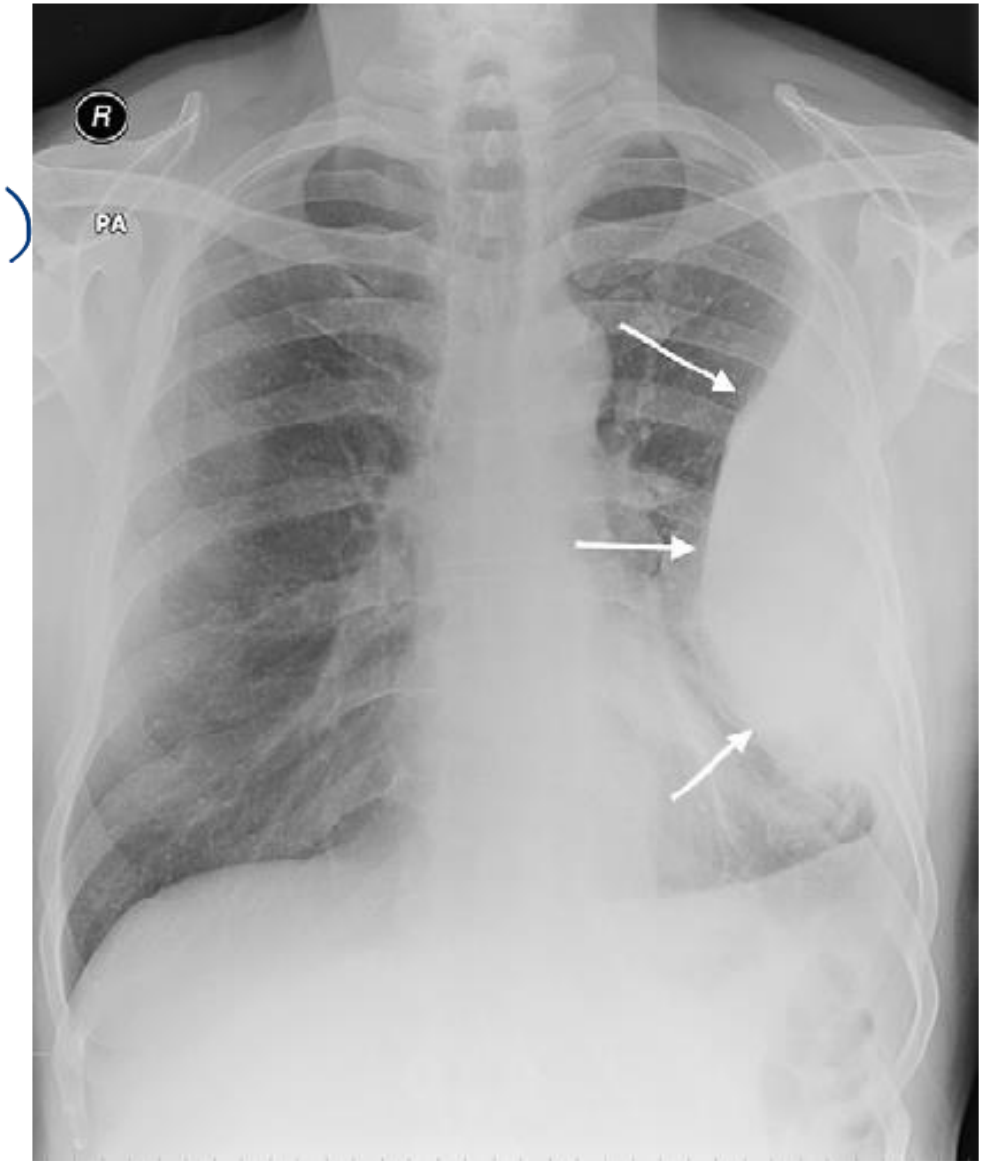
- Increasing incidence with mortality between 10 – 20%
    - 1/3 fail medical management & require surgical drainage
    - 25% require prolonged hospital admission
- Standard treatment
    - Appropriate antibiotics
    - Drainage of infected pleural fluid
    - Intrapleural catheter with or without Fibrinolytics and DNAase → TPA/Streptokinase
    - Video-assisted thoracoscopic drainage (If failed)
    - Open thoracotomy/decortication (If doesn't work)



If an empyema does not rupture, death will occur - Hippocrates

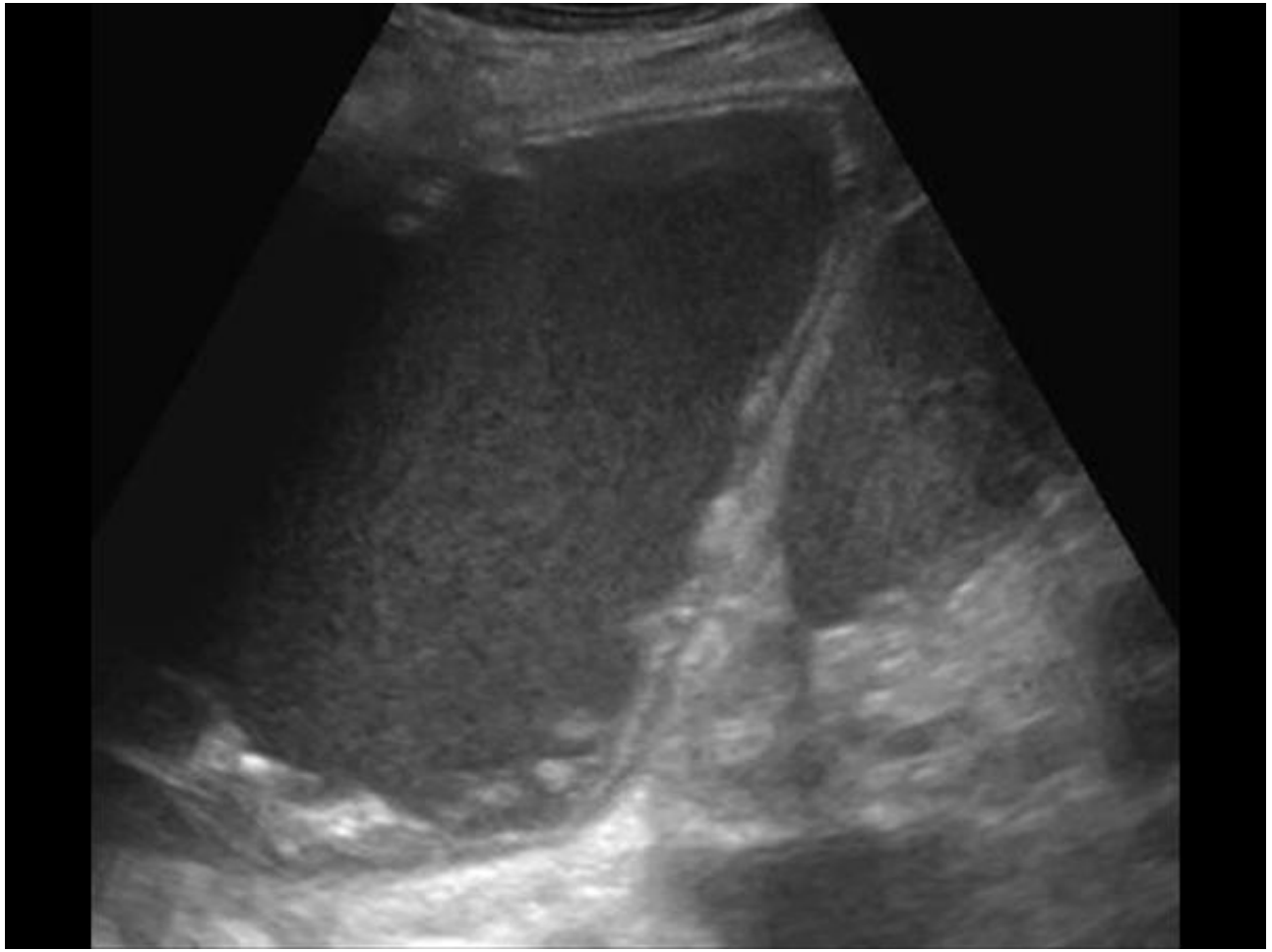
Septations (Long-time effusions/hemothorax)

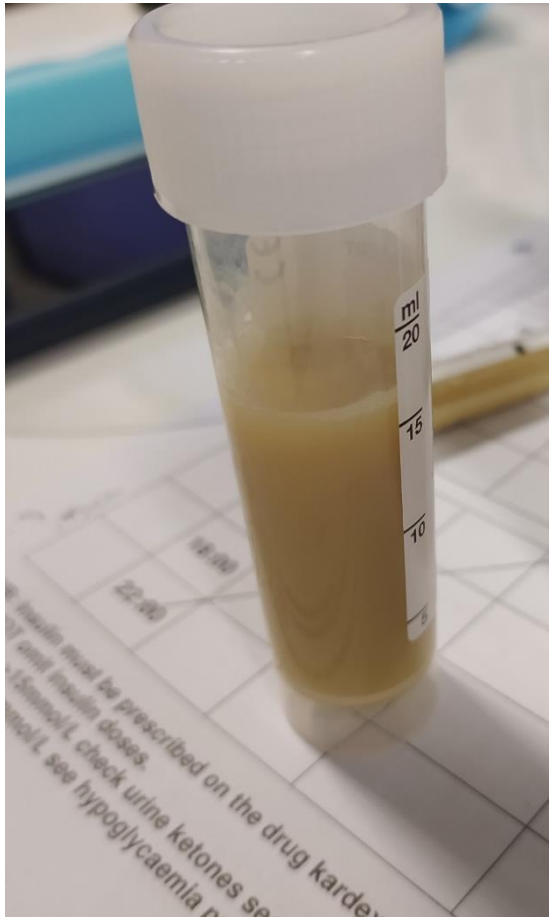




Loculated (Reverse D-Sign)

Empyema



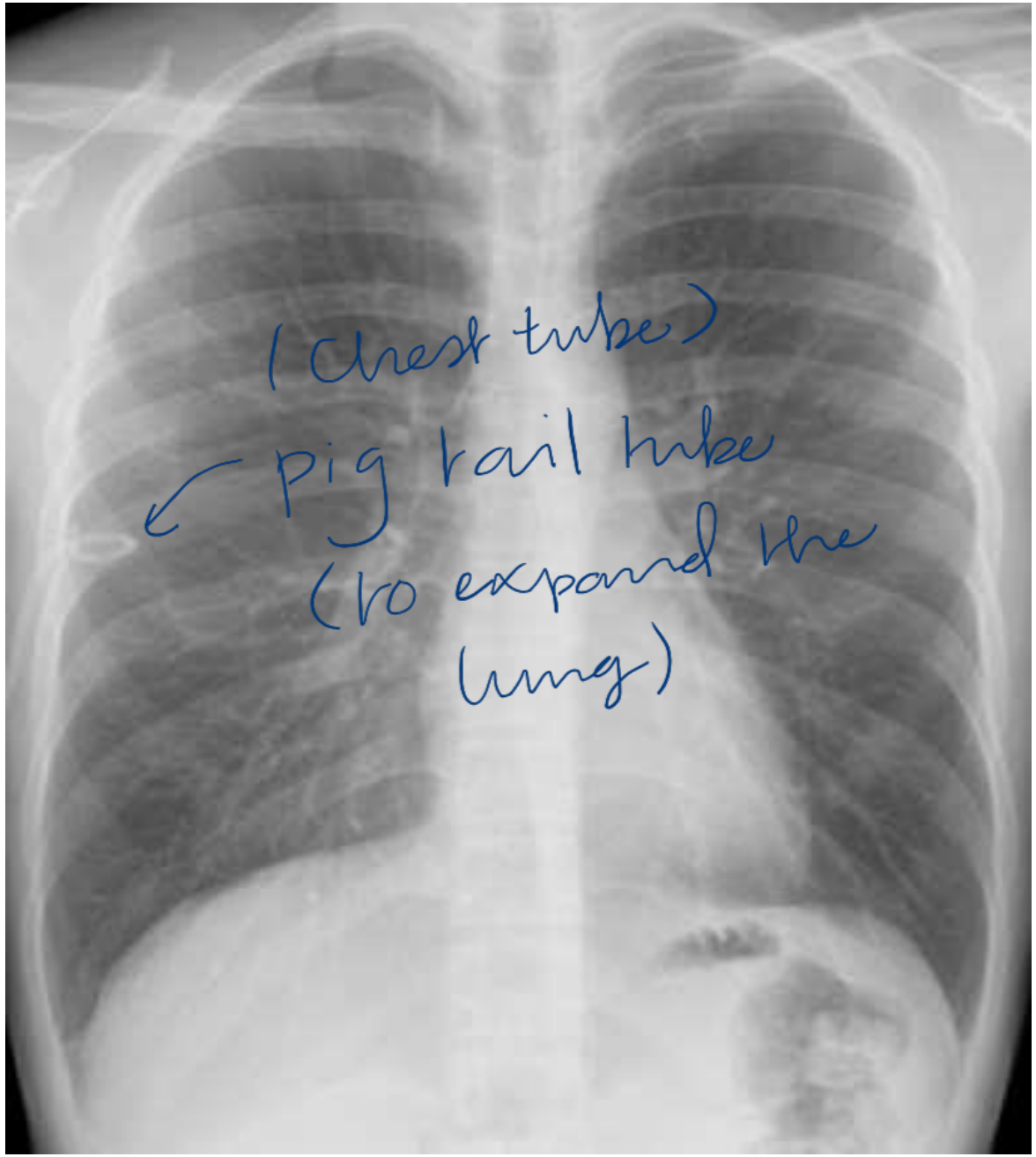


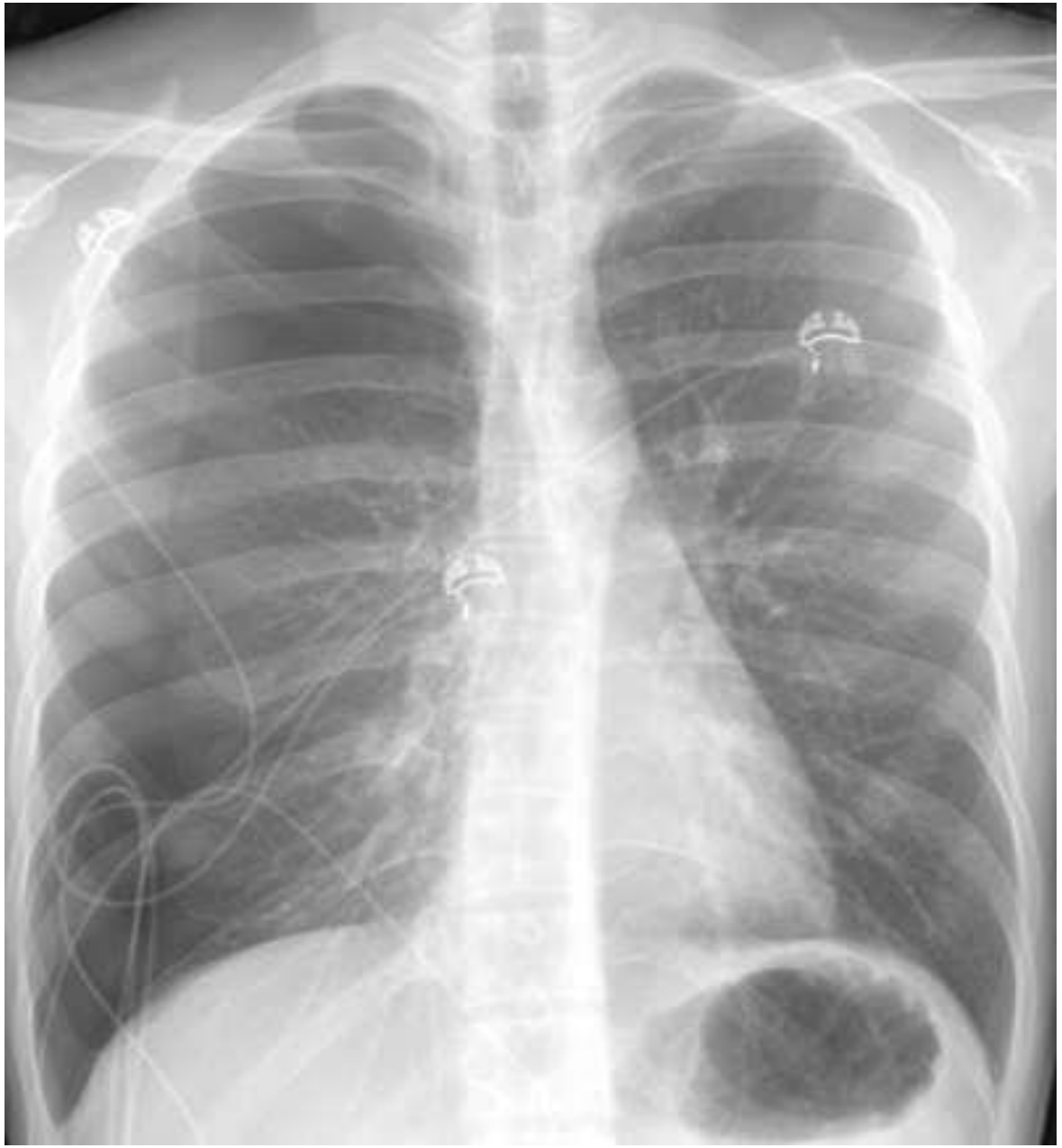
TB pleural effusion

- 5 meta-analyses have shown high accuracy of ADA in diagnosis of TB effusions - Pooled sensitivities & specificities of 88 – 92%
- Pleural fluid ADA may also be elevated in parapneumonic, rheumatoid, lymphomatous and malignant effusions

Combination with other factors recommended

- Lymphocytic predominant effusion
- Pleural fluid interferon-gamma levels
- Interferon gamma releasing assays
- Quantiferon-TB Gold & T-SPOT.TB – High rate of false positives and false negatives in pleural fluid


(chest tube)
pig tail tube
(to expand the
lung)

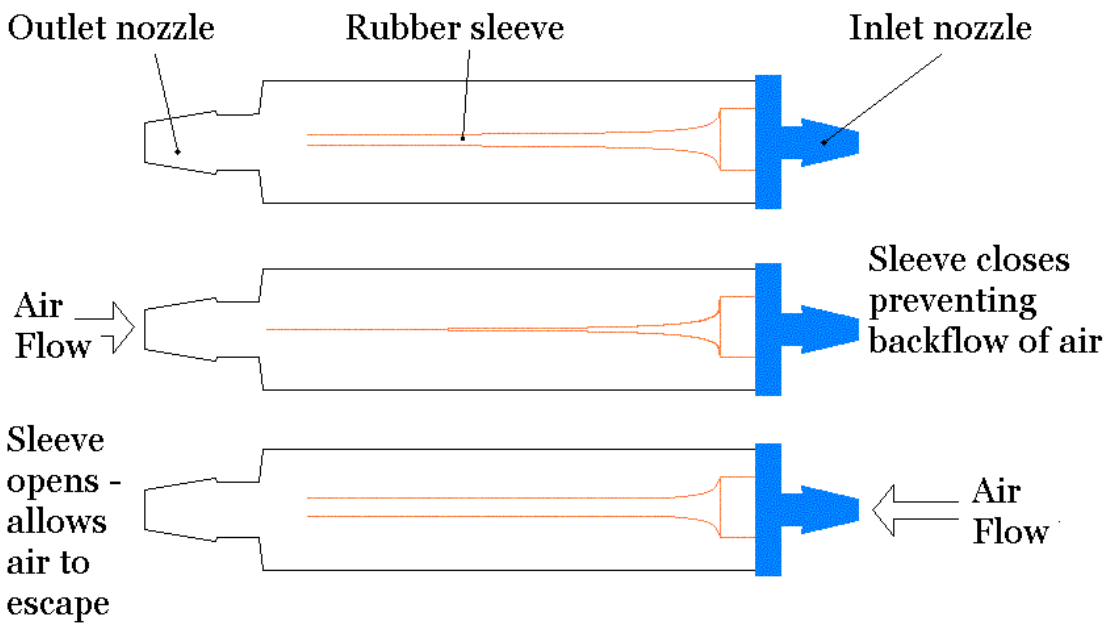


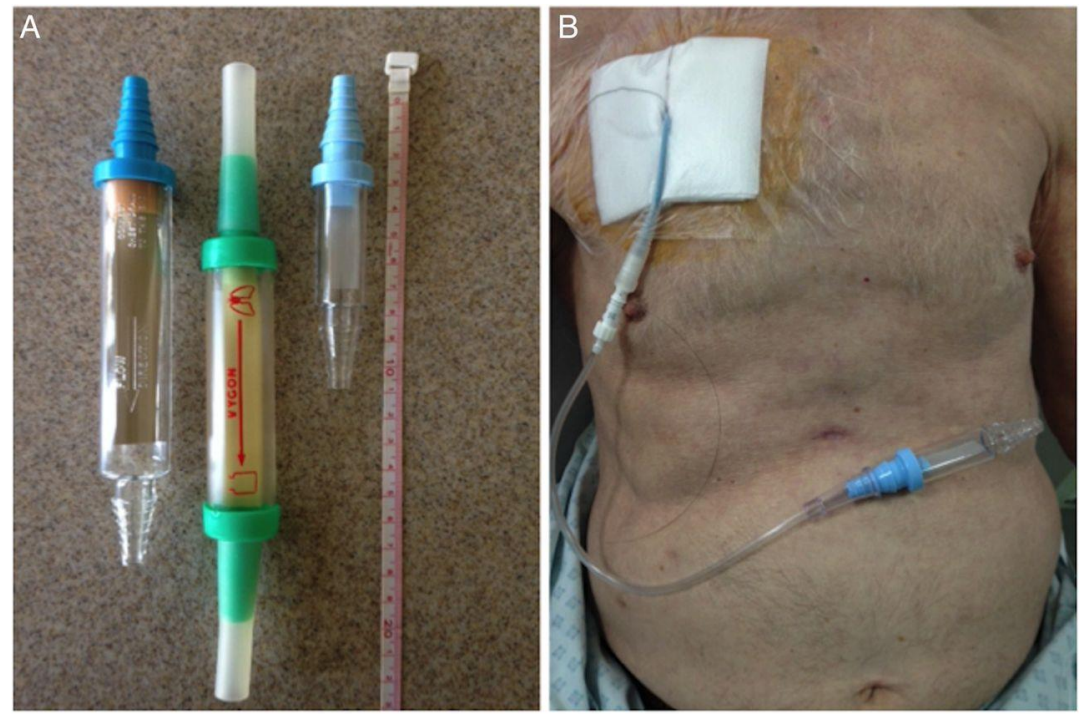
Pneumothorax

↳ primary spontaneous pneumothorax.

- Primary (PSP) = No precipitating event, no clinically apparent lung disorder
    - Men more commonly then women (tall, men , smoker)
- Secondary (SSP) = Underlying pulmonary disease present, usually COPD
- ACCP Consensus Recommendations for management of adults with primary or secondary pneumothoraces (*CHEST 2001; 119:590-602)*
- PSP – Clinically stable with small ptx (< 3cm apex-cupola distance)
    - Observe in ED for 3-6 hours; May discharge home if repeat CXR excludes progression; Followup in 12hours – 2 days with CXR
- PSP – Clinically stable with large ptx (≥ 3cm apex-cupola distance)
    - Re-expand lung with small-bore catheter (≤ 14F) or placement of 16 – 22F chest tube attached to Heimlich valve or water seal

↳ A one-way valve عشان الهوا يطلع وما يرجع يدخل


Outlet nozzle
Rubber sleeve
Inlet nozzle
Air Flow
Sleeve closes preventing backflow of air
Sleeve opens - allows air to escape
Air Flow


A
B

Primary Pneumothorax

- Persistent air leak – continued observation (3 – 5 days)

  If persist, consider surgical intervention to close air leak, pleurodese
- Pneumothorax recurrence prevention
  - Except for pts with persistent air leaks, procedures to prevent recurrence of PSP should be reserved for second ptx recurrence

    Thoracoscopy with sclerosing agents
- Pts with apical bullae should undergo bullectomy (staple bullectomy)
- No recommendation for routine use of CT-imaging in first-time PSP

Secondary pneumothorax

- SSP – Clinically stable with small ptx
    - Hospitalize pt; not managed in ED with observation or simple aspiration
    - Hospitalized pts may be observed or treated with chest tube depending
- SSP – Clinically stable with large ptx
- Placement of chest tube & hospitalized
    - Chest tube management
    - Size depends on clinical circumstances; chest tube to water seal with or without suction
    - PTX recurrence prevention
    - Medical or surgical thoracoscopy
    - Staple bullectomy

Recurrent spontaneous pneumothorax

- Estimates range from 25 – 50%; most within first year
- Female gender, tall stature (Marfan's syndrome), low body weight, & failure to stop smoking have increased risk of recurrence
- Birt-Hogg-Dubé syndrome
    - Autosomal dominant; benign skin tumors (fibrofolliculomas = benign
        - hamartomatous tumors of hair follicles) & bilateral, multi-focal kidney cancer
- Multiple pulmonary cysts – 25% ptx
- Mutations in folliculin gene localized to short arm of chromosome 17
- Loss of function tumor suppressor gene

(very rare)

Malignant Pleural effusion

- MPE most commonly exudative & symptomatic (5% transudative)

Lung (most commonly adenocarcinoma), breast, lymphoma,

- unknown primary, genitourinary, & gastrointestinal carcinomas
- Paramalignant effusions associated with malignancy but cytology neg No enough malig. cells
- Symptoms include dyspnea, orthopnea, cough; negative impact on QOL
    - Treatment focused on palliation given poor prognosis
    - Most frequent options include:

    -Repeated thoracentesis

    -Tube thoracostomy Chest tube

    - Pleurodesis

    -Tunneled pleural catheters ✓ if failed

Hemothorax

- Hemothorax is a collection of blood in the pleural cavity usually from traumatic injury
- Bloody pleural vs Hemothorax – Hct >50%
- Hemorrhage leading to a hemothorax can originate from the chest wall, intercostal vasculature, internal mammary arteries, great vessels, mediastinum, myocardium, lung parenchyma, diaphragm, or abdomen
- After placement of chest tube
  - 0-400cc Minimal
  - 400-1000cc Moderate
  - >1000cc Massive

Hemothorax

- Etiology
  - Spontaneous (coagulopathic, vascular, neoplastic, and miscellaneous)
  - Traumatic (blunt or penetrating injury)
  - Iatrogenic
- Diagnosis
  - Chest X ray
  - Ultrasound
  - CT with IV contrast (identify additional injury in 20-30%)
- Management
  - In stable patients, hemothorax less than 400cc can be managed conservatively
  - Thoracentesis can be consider in symptomatic patient or for diagnosis
  - OR → Tube Thoracostomy
  - VAT (early vs late ie >7 days)

Hemothorax

- Hemothorax less than 300cc tend to resolve spontaneously
- Retained hemothorax if not drained can lead
  - Pleural effusion
  - Infection
  - Trapped lung/fibrothorax

Mesothelioma

- Arises from mesothelial surfaces of pleural, peritoneal cavities & pericardium
- Inhalational exposure to asbestos clearly established as predominant cause of malignant mesothelioma – first etiologic connection 1960
- 70% of cases associated with documented asbestos exposure
- Asbestos miners, workers, plumbers/pipefitters, mechanical engineers, ship/boat building & repairing – high risk occupations
- Lifetime risk of mesothelioma among asbestos workers 8 – 13%
- Latency period about 30 – 40 years
- Unclear whether dose-response relationship

Mesothelioma

- Progressive growth = partial or complete encasement of lung with rinds of pleural tumor
- Minimal lung parenchyma penetration
- Spreads along interlobar fissures, diaphragm, mediastinum, pericardium
- **4 major histologic subtypes**
    - Epithelioid – most common
    - Sarcomatoid – fibroblastic-like spindle cells; may mimic fibrosarcoma
    - Desmoplastic – densely collagenized tissue with atypical cells arranged in "patternless" pattern (Bland tumor so differentiating from fibrous pleuritis difficult)
    - Biphasic – both epithelioid & sarcomatoid components (Each at least 10% of tumor)

Mesothelioma

A

B

"رب إني لما أنزلت إليّ من خير فقير".