Pathophisyolpgy of empema

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pleura

- The pleura is the serous membrane that covers the lung parenchyma, the mediastinum, the diaphragm, and the rib cage.
- This structure is divided into the **visceral** pleura and the **parietal** pleura.

visceral pleura

- The covers the **lung parenchyma**, and the interlobar fissures

Parietal pleura

- the **parietal pleura** contact with the chest wall, diaphragm, and mediastinum

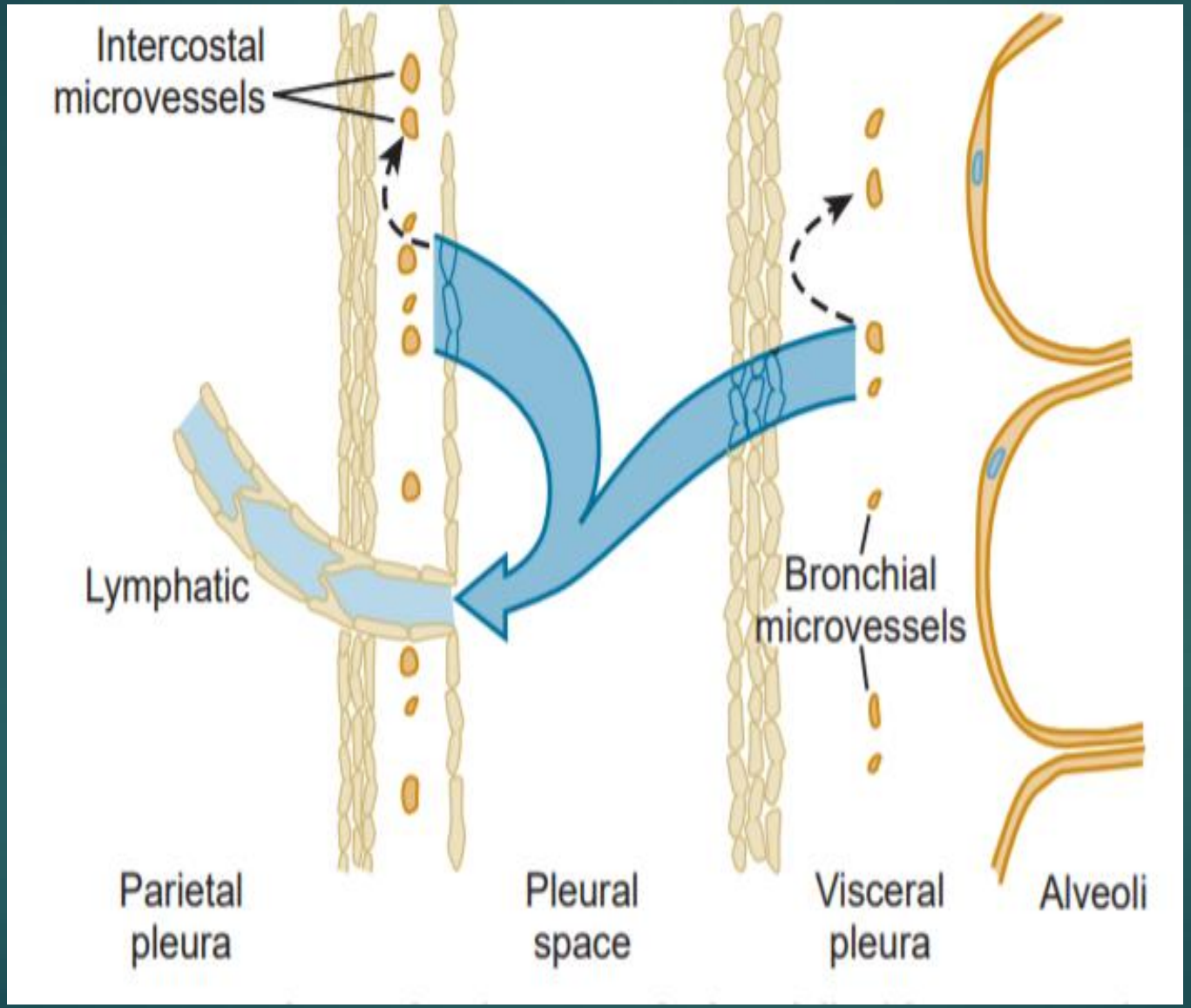
- Into this space, normal liquid and protein enter from the systemic circulation and are removed by the parietal pleural lymphatics.

Visceral pleural anatomy

- characterized by a single layer of **mesothelial cells** that have microvilli extending from their surface into the pleural space
- Species with a thick visceral pleura has an arterial blood supply from the systemic circulation, via bronchial arteries

The parietal anatomy

- pleura cover the ribs and intercostal spaces is composed of loose, irregular connective tissue covered by a single layer of **mesothelial cells**. Within the pleura are blood vessels, mainly capillaries, and lymphatic lacunas.


Intercostal microvessels
Lymphatic
Bronchial microvessels
Parietal pleura
Pleural space
Visceral pleura
Alveoli

- Normally there is **little or no contact across the pleural space** because the microvilli that extend from the parietal and visceral mesothelial cells are only 3 to 5 μm long

- The pleural space lies between the lung and the chest wall and normally contains a **very thin layer of fluid**, which serves as a coupling system. A pleural effusion is present when there is an excess quantity of fluid in the pleural space.

- This thin layer of fluid acts as a **lubricant** and allows the visceral pleura covering the lung to slide along the parietal pleura lining the thoracic cavity during respiratory movements.

volume

- the mean amount of fluid in the right pleural space in normal individuals is **8.4 ± 4.3 mL**. Normally
- the volume of fluid in the right and left pleural spaces is quite similar

cell

- They reported that the mean white blood cell count was **1 ,716 cells/mm3**
- the mean red cell count was approximately

700 cells/mm3

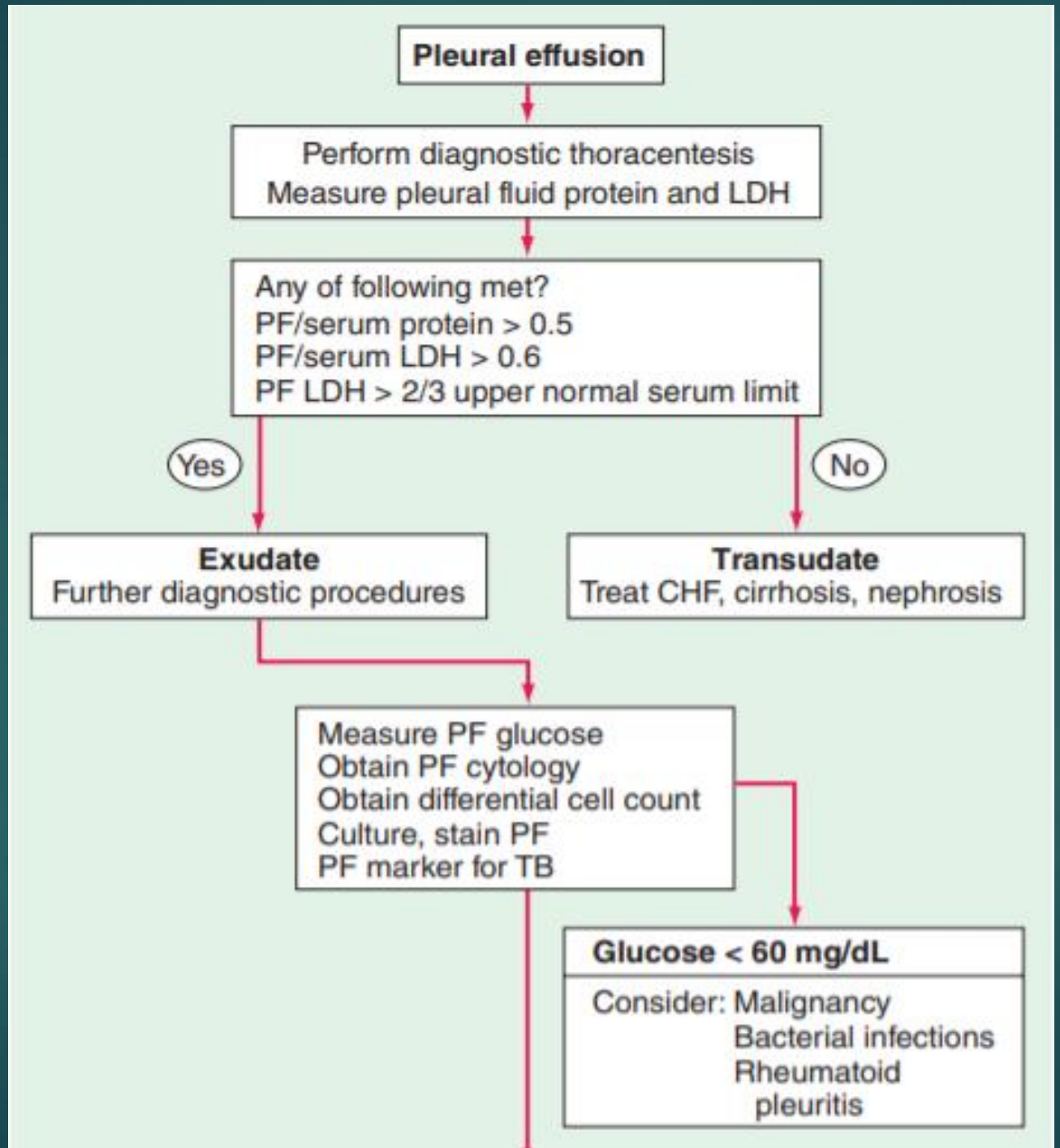
- **75%** of the cells in the pleural fluid are macrophages
- **25%** are lymphocytes,
- mesothelial cells, neutrophils, and eosinophils accounting for less than **2%** each

Pleural effusion

- entry rate of liquid must increase
- the exit rate must decrease

Pleural tap

- appearance of the fluid,
- glucose level
- differential cell count
  microbiologic studies
- cytology


Pleural effusion
Perform diagnostic thoracentesis
Measure pleural fluid protein and LDH
Any of following met?
PF/serum protein > 0.5
PF/serum LDH > 0.6
PF LDH > 2/3 upper normal serum limit
Yes
No
Exudate
Further diagnostic procedures
Transudate
Treat CHF, cirrhosis, nephrosis
Measure PF glucose
Obtain PF cytology
Obtain differential cell count
Culture, stain PF
PF marker for TB
Glucose < 60 mg/dL
Consider: Malignancy
Bacterial infections
Rheumatoid pleuritis

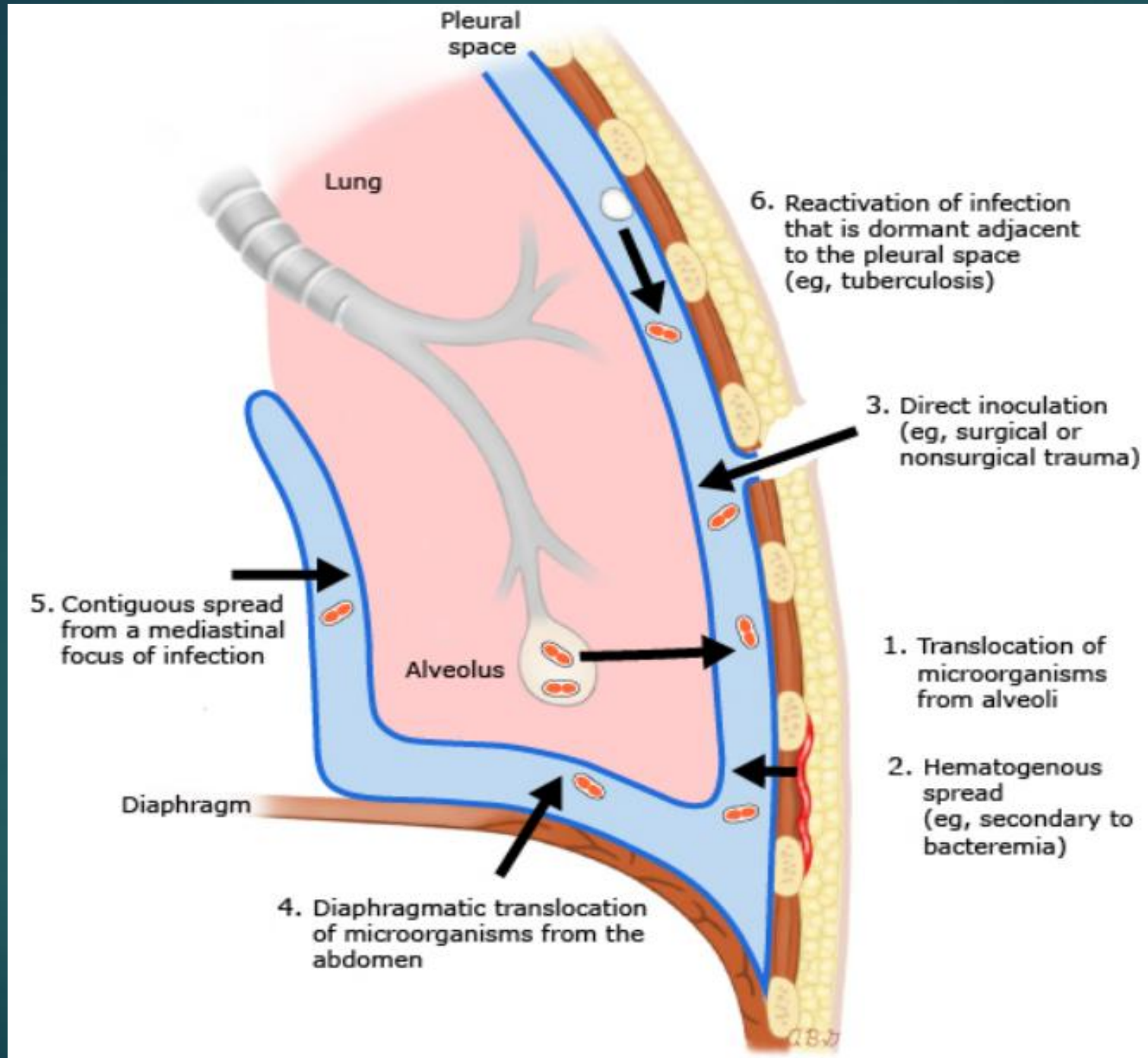
- **Parapneumonic eusions** are pleural efusions that form in the pleural space adjacent to a bacterial pneumonia. They are found in at least 40 percent of bacterial pneumonias

PATHOPHYSIOLOGY OF PLEURAL INFECTION

- The development of the initial effusion is due to **increased permeability of the pleural membranes** in response to inflammation in the underlying lung parenchyma, which is thought to result in transfer of interstitial fluid across the visceral pleura

Table 23.1 Frequency and cause of 701 patients with pleural infection[20,42,46–48]

Causes of pleural space infection	Frequency (%)
Parapneumonic effusion	70
Postbacterial pneumonia	
Hospital-acquired pneumonia	
Primary empyema	4
Postoperative	12
Traumatic	3
Blunt trauma	
Penetrating trauma	
Iatrogenic	4
e.g., Post chest tube insertion	
Abdominal infection	2
e.g., Subphrenic abscess	
Miscellaneous	5
Esophageal perforation	
Bacteremia	
Rupture of lung abscess into pleural space	
Intravenous drug abuse (contaminated needles)	


Pleural space
Lung
6. Reactivation of infection that is dormant adjacent to the pleural space (eg, tuberculosis)
3. Direct inoculation (eg, surgical or nonsurgical trauma)
5. Contiguous spread from a mediastinal focus of infection
Alveolus
1. Translocation of microorganisms from alveoli
2. Hematogenous spread (eg, secondary to bacteremia)
Diaphragm
4. Diaphragmatic translocation of microorganisms from the abdomen

Parapneumonic pleural efusions are divided into three groups

- Uncomplicated parapneumonic eusion
- Complicated parapneumonic eusion
- Thoracic empyema

Uncomplicated parapneumonic eusion

- The pleural fluid is characterized by "**exudative**" chemistries and an inux of **neutrophils** into the pleural space.
- it resolves with resolution of the pneumonia.

- fluid moves into the pleural space due to locally increased capillary vascular permeability and the activation of immune processes such as neutrophil migration.

Proinflammatory cytokines

- **(IL)-6, IL-8, (TNF-a)**
- produce changes in the anatomical shape of pleural mesothelial cells creating intercellular “gaps,” which further enhance permeability and allows the accumulation of additional fluid

exudative pleural effusions

1. Pleural fluid protein/serum protein >0.5
2. 2. Pleural fluid LDH/serum LDH >0.6
3. 3. Pleural fluid LDH more than two-thirds the normal upper limit for serum

Complicated parapneumonic eusion

- bacterial invasion of the pleural space

lysis of neutrophils increases the lactatedehydrogenase concentration in the pleural uid to values often in excess of **1000 IU/L**

Thoracic empyema

- Empyema develops when there is evident bacterial infection of the pleural liquid, resulting in either **pus or the presence of bacterial organisms on Gram stain.**

empyema

1. Loculated pleural fluid
2. Pleural fluid pH <7.20
3. Pleural fluid glucose (<60 mg/dL)
4. Positive Gram stain or culture of the pleural fluid
5. Presence of gross pus in the pleural space

EVOLUTION OF INFECTION: "THE FIBROPURULENT PHASE"

- If inflammation persists within the lung parenchyma, secondary bacterial invasion of the pleural space can occur with profound pathological effects on the normal pleural physiology.

- The usual parapneumonic eusion is small and resolves with appropriate antibiotic therapy.

- However, if bacteria invade the pleural space, a complicated parapneumonic eusion or empyema may result, which will require antibiotic therapy plus additional interventions.

- The high levels of fibrinolytic activity, which characterize the normal pleural space, are rapidly depressed and titers of specific inhibitors of fibrinolytic activity such as tissue plasminogen activator inhibitor (PAI) 1 and 2 rise

- Levels of PAI 1 and 2 and mediators such as TNF-a are directly released from mesothelial cells and are **increased in infected** pleural fluid compared with fluid from malignancy and other causes

- This leads to **fibrin deposition** over the visceral and parietal pleura with division of the pleural space by fibrinous septae, producing fluid loculation and pleural adhesions

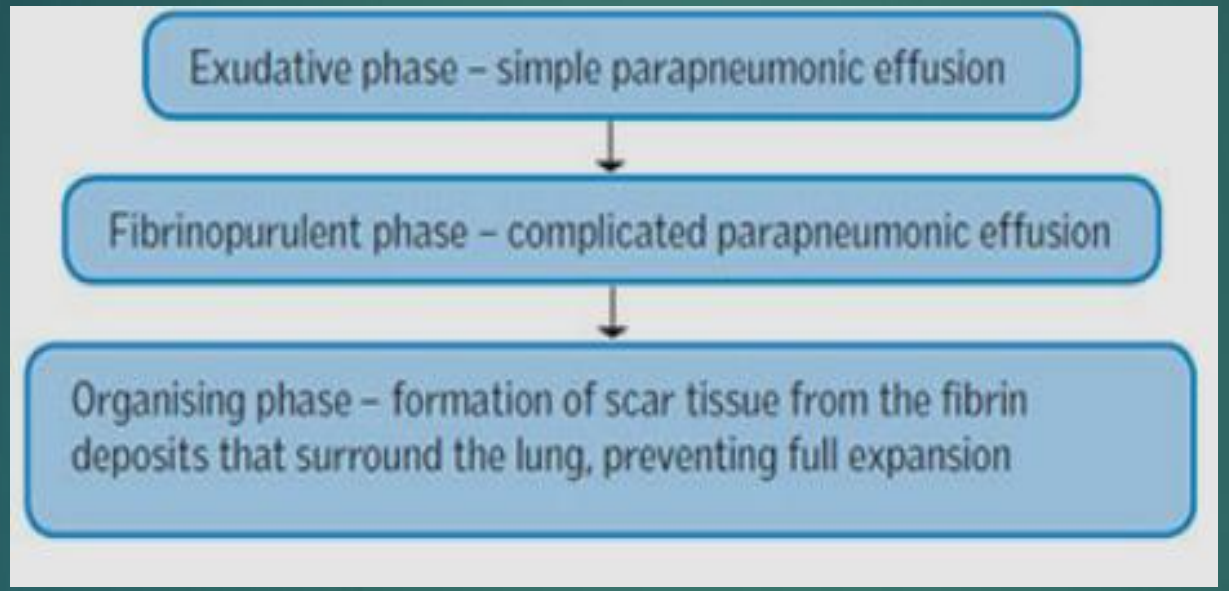
- . Although effusions of any cause may become loculated, depression of the fibrinolytic system (elevated PAI level, depressed tissue plasminogen activator [tPA]) has only been observed in pleural infection and not in effusions secondary to malignancy or transudates.6

- **Bacterial metabolism and neutrophil phagocytic activity induced** by bacterial cell wall–derived fragments and proteases lead to increased lactic acid productionand thus a fall in pleural fluid pH and glucose—the biochemical hallmarks of early transition to the infected state.

- ultimately the pleural fluid becomes frankly purulent,secondary to bacterial and inflammatory cell death and lysis.

NATURAL HEALING: "THE ORGANIZING STAGE"

- Finally, there is the proliferation of fibroblasts and the evolution of **pleural scarring**, with animal model data suggesting this process is driven by mediators such as **platelet-derived growth factor and transforming growth factor beta (TGF-β)**


Exudative phase – simple parapneumonic effusion
Fibrinopurulent phase – complicated parapneumonic effusion
Organising phase – formation of scar tissue from the fibrin deposits that surround the lung, preventing full expansion

- This forms an **inelastic peel** on both pleural surfaces with dense fibrous septations across the pleural cavity. As this solid fibrous peel replaces the soft fibrin, **lung reexpansion is prevented**, impairing lung function.

- Interesting evidence points to a potential therapeutic target in the mediators thought to drive this process with the administration of **anti-TGF-β antibodies** during pleural infection resulting in significantly less pleural thickening in a well-established animal model of empyema.

- In empyema, deposition of fibrin begins early and is aggressive, and within **a few weeks a thick layer of collagen** (referred to as ‘rind’ or ‘peel’) is deposited on both pleural spaces. If left untreated the process continues until pleural fibrosis causes contraction of the chest wall and lung **(fibrothorax)**

Table 23.2 Light's classification of parapneumonic effusions and empyema

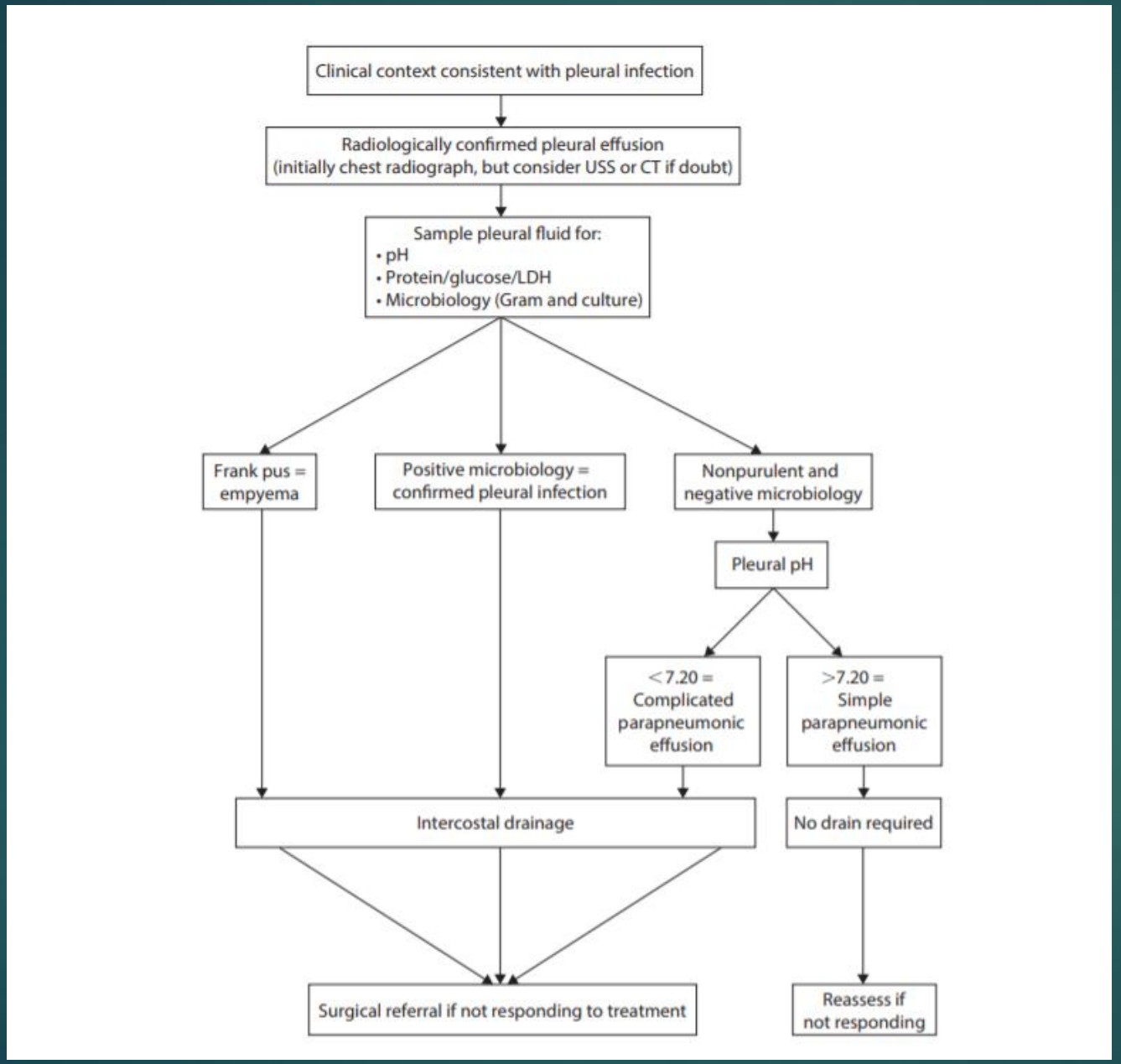
	Parapneumonic effusion
Class 1—Nonsignificant	Small <10 mm thick on decubitus No thoracentesis needed
Class 2—Typical parapneumonic	>10-mm thick Glucose >40 mg/dL, pH >7.2, Gram's stain and culture negative
Class 3—Borderline complicated	pH = 7.0–7.2 or LDH >1000 Gram's stain negative and culture negative
Class 4—Simple complicated	pH <7.0 Gram's stain or culture positive Not loculated or frank pus
Class 5—Complex complicated	pH <7.0 Gram's stain or culture positive Multiple loculation
Class 6—Simple empyema	Frank pus Single locule or free flowing
Class 7—Complex empyema	Frank pus, multiple loculations Often requires decortication

EMPYEMA

- Empyema correlates to the late fibrinopurulent stage and is defined as **frank pus** in the pleural space (i.e., macroscopic evidence of bacterial and inflammatory cell death) regardless of biochemical and microbiological parameters

Table 23.3 Pleural fluid characteristics according to stage of pleural infection

	Simple parapneumonic effusion	Complicated parapneumonic effusion	Empyema
Appearance	May be turbid	May be cloudy	Pus
Biochemical markers	pH >7.30 LDH may be elevated Glucose >60 mg/dL or glucose pleural/serum ratio >0.5	pH <7.20 LDH >1000 IU/L Glucose <35 mg/dL	n/a
Nucleated cell count	Neutrophils usually <10,000/μL	Neutrophils abundant (usually >10,000/μL)	n/a
Gram's stain	Negative	May be positive	May be positive
Culture	Negative	May be positive	May be positive


Clinical context consistent with pleural infection
Radiologically confirmed pleural effusion (initially chest radiograph, but consider USS or CT if doubt)
Sample pleural fluid for:
• pH
• Protein/glucose/LDH
• Microbiology (Gram and culture)
Frank pus = empyema
Positive microbiology = confirmed pleural infection
Nonpurulent and negative microbiology
Pleural pH
<7.20 = Complicated parapneumonic effusion
>7.20 = Simple parapneumonic effusion
Intercostal drainage
No drain required
Surgical referral if not responding to treatment
Reassess if not responding

THANKS