PLEURAL EFFUSION: DIAGNOSIS, MANAGEMENT AND DISPOSAL

1. This replaces the DGAFMS Medical Memorandum No.63 on Primary (Idiopathic) Pleural Effusion, which dealt with tubercular pleural effusion.

2. Normally the pleural space has 5 to 15 ml of fluid, which acts as a coupling system between the lung and chest wall. Pleural effusion is an abnormal accumulation of fluid in the pleural space as a result of disruption in the homeostatic forces that control the flow of fluid into and out of the pleural space.

3. **Exudative and Transudative pleural effusions:** Exudative pleural effusion occurs when *local factors* that influence the formation and absorption of pleural fluid are altered, while transudative effusion results from the alteration of *systemic factors.* Pleural effusions are classified as exudates if they meet the following criteria:

- Turbid or purulent fluid, which clots upon withdrawal from chest.
- Fluid cytology shows WBCs > 1000/mm^3.
- Specific gravity of fluid >1018.
- Fluid glucose < 60mg/dl
- Pleural fluid protein > than 3.0 g/dl.
- Pleural fluid protein divided by serum protein > than 0.5
- Pleural fluid lactate dehydrogenase (LDH) divided by serum LDH > than 0.6.
- Fluid pH is < 7.20
- Pleural fluid LDH >than two-thirds the upper limits of normal for the serum LDH.

Causes of transudative effusion are listed in Table No.1 and those of exudative ones in Table No.2.

Table 1. CAUSES OF TRANSUDATIVE PLEURAL EFFUSIONS	
1.	Congestive heart failure
2.	Cirrhosis of liver
3.	Nephrotic syndrome
4.	Peritoneal dialysis
5.	Superior venacaval obstruction
6.	Myxedema
7.	Pulmonary emboli

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Table 2. CAUSES OF EXUDATIVE PLEURAL EFFUSIONS		
1.	INFECTIONS	Tuberculosis Bacterial infections Parasitic infections Viral infections
2.	NEOPLASTIC DISEASES	Secondary malignancy Mesothelioma
3.	Collagen-vascular diseases	Rheumatoid pleuritis Systemic lupus erythematosus
4.	Pulmonary infarction	
5.	Gastrointestinal disease	Pancreatic disease Intraabdominal abscess esophageal perforation
6.	Post-cardiac injury syndrome	
7.	Asbestos exposure	
8.	Drug-induced pleural disease	Nitrofurantoin Dantrolene Methysergide
9.	Miscellaneous	Radiation therapy Electrical burns Iatrogenic injury Pericardial disease Hemothorax

4. **Approach to the patient:**

(a) Clinical History: Symptoms suggestive of any of the etiologic conditions mentioned above must be noted. While 15% of patients may be asymptomatic, common symptoms are:

(i) Chest Pain: Inflammation of the pleura is manifested by pleuritic chest pain, localized over the affected area. It is sharp in nature and often the patient describes an end inspiratory "catch" and stops inhaling any further. The pain may be referred to the abdomen or on to ipsilateral shoulder. As effusion sets in, the pain may decrease in intensity. A dull, aching chest pain may suggest pleural malignancy.

(ii) Cough: It is dry and non productive, which is presumed to result from pleural inflammation or collapsed bronchial walls.

(iii) Dyspnea: Pleural fluid occupies volume inside the thorax, leading to the restriction of lung volumes. Chest pain with the resultant splinting and concomitant lung parenchymal disease may add to the dyspnea. The symptoms are more manifest where the quantity of fluid is large.

(b) Physical examination:

(i) Size of hemithorax and respiratory movements: Increase in the intra-pleural pressure leads to

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enlargement of the hemithorax. Usual concavity of intercostal spaces appears blunted or even bulging. In those cases where the intra-pleural pressure is decreased (e.g. major bronchus obstruction as in neoplasms), the normal concavity of intercostals spaces are aggravated and hemithorax may be smaller. In either situation, the expansile movement of the hemithorax is invariably decreased on the ipsilateral side.

(ii) Position of trachea indicates the relationship between the pleural pressures in the two hemithoraces. Trachea may be central if there is ipsilateral bronchial obstruction or mediastinum is fixed due to disease. Tactile vocal fremitus is attenuated over the areas where fluid separates lung from the thoracic cage. This sign helps in establishing the extent of effusion and locate site for thoracentesis. Shift in the apical impulse of heart may also be observed where fluid collection is sizeable. Localized intercostal tenderness in a febrile patient with pleural effusion must raise the strong suspicion of empyema thoracis.

(iii) Percussion note over a pleural effusion produces characteristic 'stony dull' or flat note. Maximum dullness is observed at the lung bases where thickness of fluid is the greatest. The upper limit of dullness is at least a space higher in the axilla compared to the limits of dullness anteriorly and posteriorly. Because of the shape of the upper border of dullness, this is called Ellis's 'S' curve, a phenomenon, which can also be observed radiologically. Shift in the dull note with posture indicates free pleural fluid, as against loculated effusion, where the dullness does not shift. Care must be taken to differentiate the shifting dullness of a pleural effusion with that of hydropneumothorax where the upper level of dullness is horizontal.

(iv) Auscultation shows decreased or absent breath sounds over the effusion. As the lung near the superior border of fluid is partially atelectatic, breath sounds may be bronchial in character at this point. Plural rubs are coarse, creaking, scratchy, leathery superficial sounds heard in the latter part of inspiration and early expiration with a to-and-fro pattern of the sound. They result from rubbing together of roughened pleural surfaces during respiratory movements. They disappear during breath holding. As effusion appears over an area of pleuritis, the sign may disappear and later reappear as the effusion regresses. While listening with the stethoscope at the superior level of a hydropneumothorax,

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a distinct splash may be audible if the patient is gently shaken (succussion splash).

(v) Spirometry: Pleural effusion induces restriction of all lung volumes. However, mild to moderate effusions may not show proportionate restrictive defect, as compensation occurs by healthy side.

(d) Thoracic imaging

(i) Plain X-ray chest PA view shows classical feature of homogenous density of lower hemithorax with a concave upper border. The superior point of density laterally in the axilla is often two spaces higher than its medial level. The costophrenic and cardiophrenic angles are obliterated. Lateral view demonstrates a homogenous opacity, separating lung above from the gas shadow in the fundus of the stomach below over the left side. Loculated pleural effusion may produce opacity with `D' shape (the convexity of facing the lung) or a density with 'tear-drop' shape. In a few cases, the lung may float above the fluid, where the pleural effusion is called subpulmonic effusion.

(ii) Ultrasonography (USG) of thorax can confirm, quantify and localize pleural fluid collection and also help in its aspiration.

(iii) Computed tomographic scan of the thorax is an investigation which can delineate the pleural effusion and to some extent its characteristics.

(e) Thoracentesis: Diagnostic thoracentesis is a must to arrive at the etiology. Aspiration is done in the scapular line in the 8^{th} or 9^{th} interspace. The characteristics of the common types of pleural effusions are given in Table 3. Figure No.1 gives a decision chart, which shows the flow of diagnostic approach. Physical, biochemical, cytological and microbiological characterization of tapped pleural fluid gives a diagnosis in majority of cases.

(i) Gross appearance: It may be clear, serous, serosanguinous, turbid, or frankly purulent. Its color may vary from light yellow or straw to varying shades of red, brown, yellow, or even green. It may be odorless or foul smelling. Hemorrhagic pleural fluid suggests underlying malignancy, trauma or pulmonary infarction. Some cases of tubercular pleural effusion and pneumonia may show blood-tinged fluid. As 2 ml of blood can convert a pleural effusion to hemorrhagic effusion, iatrogenic and other types of trauma also could lead to this type of pleural fluid.

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(ii) Cytology: Differential leukocyte count helps in supporting the diagnosis. Tubercular effusion has predominant lymphocytes, while predominance of polymorphonuclear leucocytes points to a bacterial infection. Mesothelial cells are never seen in tuberculosis. Possibility of mesothelioma must be ruled out in such cases. Care must be taken to see that the cytology technician does not mistake malignant cells (which are hyperchromatic) to be lymphocytes. All cytology slides must be preserved and reviewed by the pathologist.

(iii) Measurements of pleural fluid specific gravity, protein content and LDH level help the diagnosis. The specific gravity is above 1018 and protein above 3g/dl in all types of infections and in malignancies.

(iv) Glucose and amylase estimation, along with bacteriological and cytological studies help to characterize different types of exudates. Reduced values (below 50mg/dl) of sugar suggest tubercular, bacterial or rheumatoid effusions. Elevated amylase must prompt the clinician to look for pancreatic diseases, rupture of esophagus or malignancy as the cause for the effusion.

(v) Additional evaluations like pleural fluid adenosine deaminase level and rheumatoid factor and tuberculin test further facilitate the differential diagnosis.

5. **Common types of pleural effusions, their management and disposal**

(a) **Tubercular pleural effusion:**

(i) This is the commonest type of effusion, necessitating treatment and follow up. The patient must be placed on standard chemotherapy as follows:

2 months daily treatment (Intensive Phase)

- Tab Isonicotinic acid hydrazide 300mg
- Cap Rifampicin 600mg
- Tab Ethambutol 1200mg
- Tab Pyrazinamide 2g

4 months daily treatment (Continuation Phase)

- Tab Isonicotinic acid hydrazide 300mg
- Cap Rifampicin 600mg

Doses mentioned are for adults weighing 50kg and above. For patients below 50kg weight, rifampicin dose is 450mg, ethambutol is 1000mg and pyrazinamide is 1.5g.

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Addition of tab prednisolone 40mg daily for the first 4-6 weeks and tapering it over the next 4-6 weeks helps in reducing the incidence of residual pleural thickening. Active physiotherapy must be started once the patient becomes afebrile, which happens in 5-15 days of starting chemotherapy. Biweekly follow up of the patient in hospital for clinical resolution is necessary for the initial 4 weeks. During this period, liver function studies can help in early detection of drug-induced hepatotoxicity. Active physiotherapy is essential.

(ii) **Follow up and Disposal**: Therapeutic tap is necessary in massive effusion with respiratory distress and in hydropneumothorax/pyopneumothorax. After clinical improvement including regression of fluid, the patient must be sent on a period of 6 weeks sick leave. On review after sick leave, repeat chest X-ray PA view, USG thorax and spirometry must be done to quantify his functional recovery. Asymptomatic patients who have recovered to 80% or more of predicted spirometric values and have no evidence of pleural fluid are to be observed in medical classification P2 for 24 weeks and re-assessed thereafter. If the spirometric values are in the range 60-79%, or radiological evidence of thickened pleura is observed, the patient must be followed up in medical classification P3 for 24 weeks, after which period he must be evaluated at a respiratory medicine center for sequel, complications or need for pleurectomy. If pleural fluid persists after 3 months of starting chemotherapy, repeat evaluation and reconsideration of etiological diagnosis becomes necessary.

(iii) **Disposal of recruits/cadets:** Personnel who are under training and also suffering from tubercular pleural effusion must be invalided out.

(b) **Bacterial infections** leading to pleural effusion (parapneumonic effusion and empyema) usually complicate lower respiratory tract infection. They must be managed by energetic, appropriate and judicious antibiotic therapy for 4-6 weeks. Repeated therapeutic aspirations are necessary to drain the pleural space completely. Tube thoracostomy or pigtail catheter drainage must be instituted in cases where:

- Pyopneumothorax is seen.
- Frank pus is aspirated from the pleural space.
- Pleural fluid glucose < 50mg/dl.
- Gram stain and/or culture positive.
- pH of the fluid <7.0 and 0.15 units less than arterial pH
- USG shows multiple loculations of fluid with debris.

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Loculated effusion may need thrombolytics in addition. Urokinase 100,000 U or streptokinase 250,000 U in 100 ml saline is introduced through the tube thoracostomy and retained for 2 hours. Insufficient duration of antibiotic therapy and inordinate delay in tube thoracostomy are the common causes of complications of this type of pleural effusion, as a free flowing pleural effusion can become loculated within a matter of hours. Inadequate pleural drainage may lead to multiple loculations and residual pleural fibrosis. Thoracoscopic breakdown of adhesions, empymectomy or thoracotomy with decortication may be required in such cases.

(viii) After antibiotic therapy, supplemented with thoracostomy where necessary, the individual needs to be sent on a period of sick leave of 4-6 weeks. On review after sick leave, the disposal is based on the guidelines given in para 5(a) (ii) and (iii).

(b) **Malignant effusions:** Carcinoma lung, carcinoma breast and lymphoma together cause 75% of malignant effusions. Most patients complain of dyspnea out of proportion to the size of effusions. Cytology and/or pleural biopsy clinch the diagnosis. Presence of effusion in a case of malignancy indicates disseminated disease, not curable with surgery or chemotherapy. Management is mainly symptomatic. Pleurodesis with talc or chemicals may help some patients. For palliative treatment, the patient is to be referred to the nearest Malignant Diseases Treatment Center.

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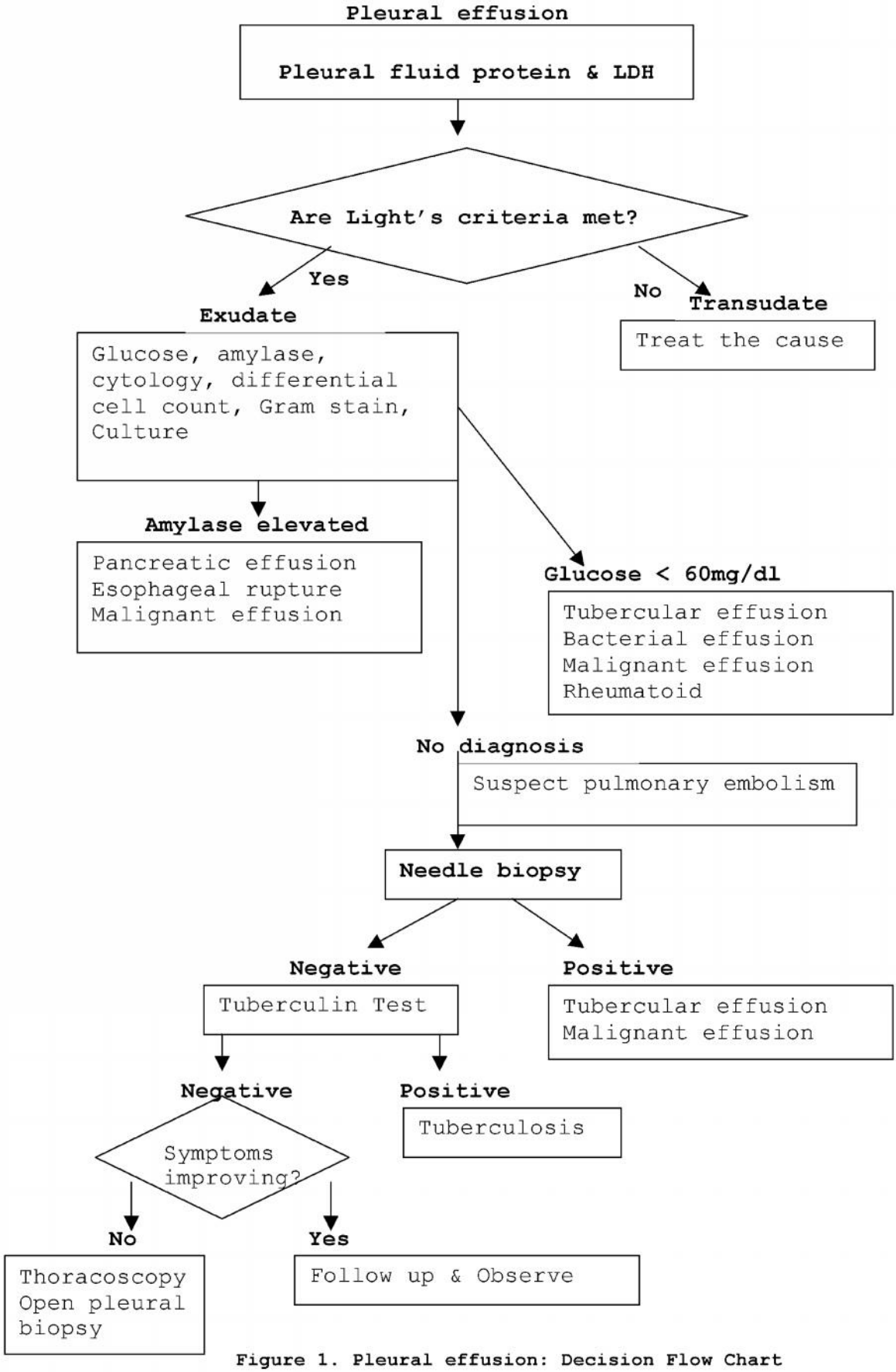

Figure 1. Pleural effusion: Decision Flow Chart

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