Pleural effusion – a diagnostic approach

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Pleural effusion is a condition commonly encountered by the physician. It may be associated with a wide variety of diseases, ranging from benign viral pleurisy to malignant effusions[1]. A proper diagnostic evaluation of a pleural effusion is important in determining its aetiology, severity and prognosis and for proper management.

Table 1. Causes of pleural effusions[1]

Transudative	Exudative
Congestive cardiac failure	Infections – Bacterial, tuberculosis, viral, fungal, parasitic
Cirrhosis	Neoplastic disease – Metastatic, mesothelioma
Nephrotic syndrome	Collagen vascular disease – Rheumatoid arthritis, SLE, Wegener's
Pulmonary infarction	Gastro-Intestinal disease – Acute pancreatic, oesophageal perforation
Myxoedema	Drug induced – Nitrofurantoin, amiodarone
	Chylothorax and pseudochylothorax
	Pulmonary infarction
	Haemothorax – Trauma, pneumothorax
	Miscellaneous – Dressler's syndrome, uraemia, Meig's syndrome, radiation, pericardial disease, yellow nail syndrome

Table 2. Leading causes of pleural effusions[1]

Congestive cardiac failure
Pneumonia
Tuberculosis
Metastatic malignancy
Cirrhosis with ascites
Viral disease

Presentation

A pleural effusion may be symptomatic or may be an incidental finding on a routine examination. The patient may complain of a pleuritic type chest pain associated with the inflammation of the overlying pleura. Large effusions may cause breathlessness by impairing gas exchange and a dry cough.

Asymptomatic effusions should be specifically sought in certain illnesses, eg: SLE, dengue, cirrhosis, lung malignancy.

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Diagnosis of a pleural effusion

When a pleural effusion is suspected, two aspects need to be considered. Firstly, the presence of a pleural effusion has to be confirmed. Next, its aetiology has to be determined.

1) Detection of an effusion

The clinical features (especially examination findings) and investigations (especially chest radiography and ultrasonography) are invaluable in detecting a pleural effusion.

• Clinical findings

Pleuritic pain chest suggests the presence of an inflammation in the pleura as well as the side involved. Physical examination is more helpful in detecting an effusion (Table 3), although signs may be absent if the effusion is small (ie: <500ml). Moderate (500-1500ml) and large (>1500ml) effusions are easily revealed by physical examination.

Table 3. Physical signs of a pleural effusion

Limited chest wall movements
Impaired vocal fremitus
Stony dull percussion note
Diminished or absent breath sounds
Diminished or absent vocal resonance
Bronchial breathing at the upper level
Mediastinal shift in large effusions.

• **Radiology**

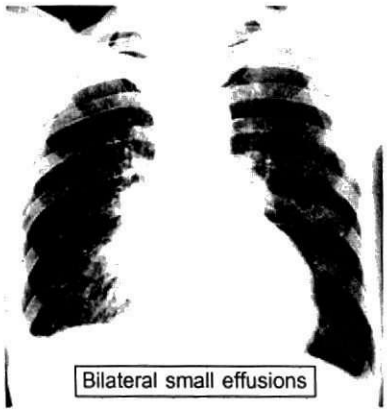
Table 4. Radiological appearances of pleural effusions

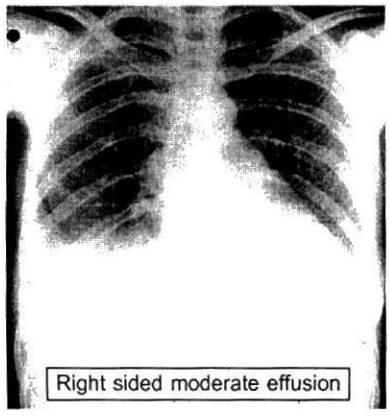
1. Free fluid
   Typical – small , moderate, massive
   Atypical – subpulmonary, lamellar, others
2. Encysted (loculated) fluid
   Fissural (interlobar) loculation
   Loculation against the chest wall

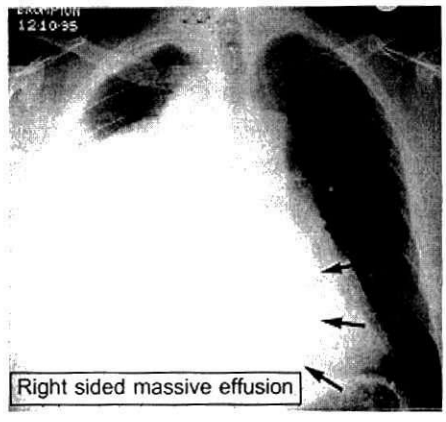
Chest radiography is a quick method of detecting pleural fluid. Moderate to large effusions are easily detected in the posteroanterior films. A pleural effusion typically appears as a homogenous opacification filling the lung bases, with a concave upper margin. To obliterate the lateral costophrenic angles, 100-200ml of free fluid is required, while the posterior costophrenic angles are obliterated with 75ml of fluid. As little as 10 ml of free fluid could be detected in a lateral decubitus chest radiograph[2].

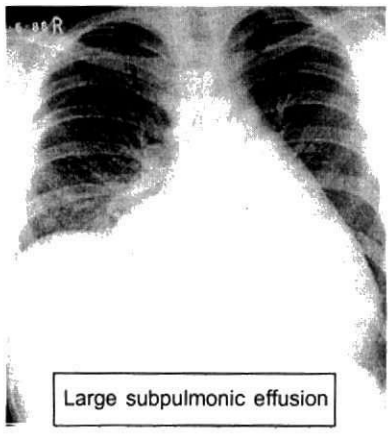
Atypical effusions, such as subpulmonic and lamellar fluid collections too can be seen in the chest radiograph.

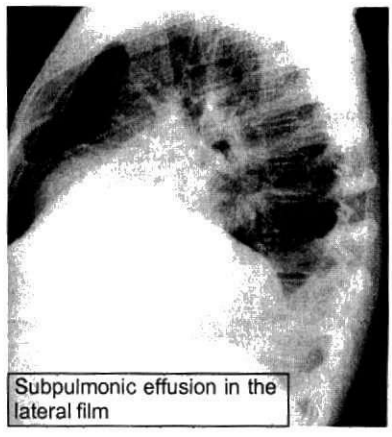
Sometimes pleural effusions become encysted or loculated. The fluid could be loculated in the fissures (interlobar) or against the chest wall. These encysted effusions are also revealed in the chest radiograph.

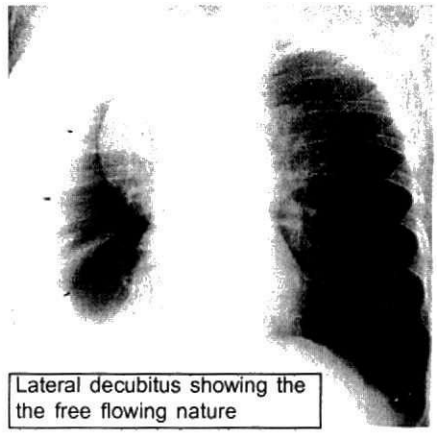

Bilateral small effusions

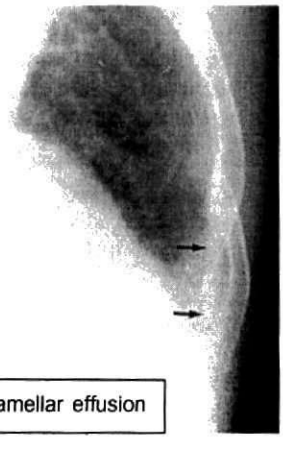

Right sided moderate effusion

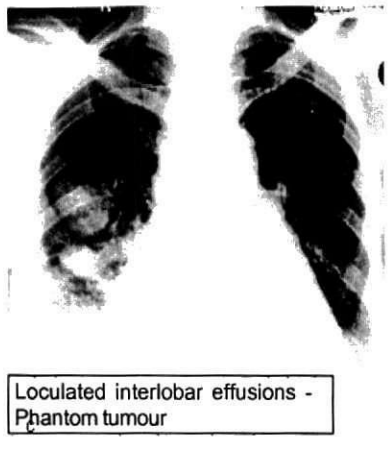

Right sided massive effusion

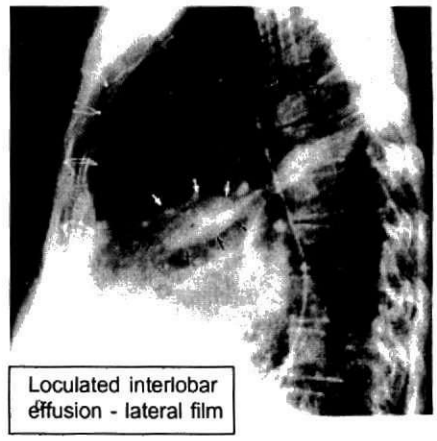

Large subpulmonic effusion

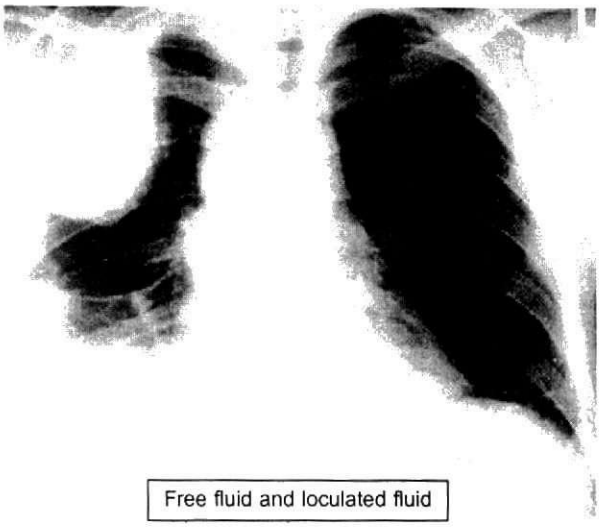

Subpulmonic effusion in the lateral film


Lateral decubitus showing the the free flowing nature

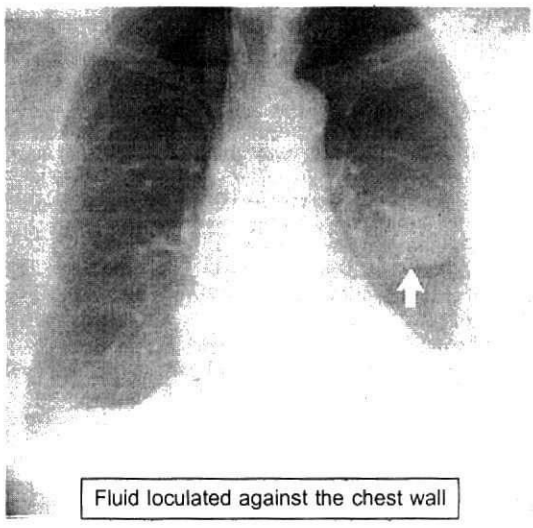

Lamellar effusion


Loculated interlobar effusions - Phantom tumour


Loculated interlobar effusion - lateral film



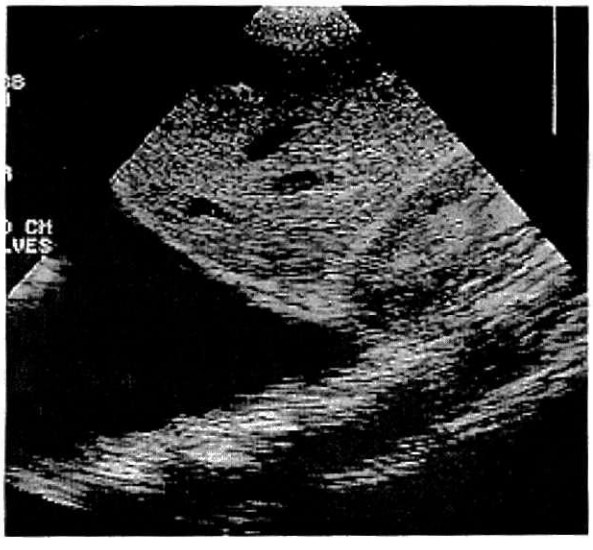
Free fluid and loculated fluid



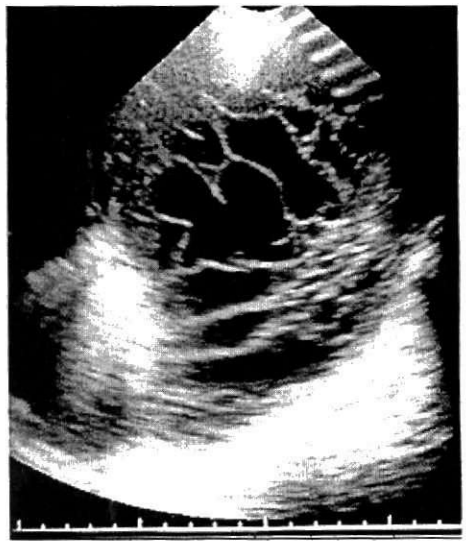
Fluid loculated against the chest wall

- **Ultrasonography**

Ultrasonography is helpful in confirming the presence of a pleural effusion as well as identifying its site. This is especially useful when identifying parapneumonic and loculated effusions. Pleural fluid appears as an echo free space between the chest wall and the lung. The presence of echoes and septation indicates an exudate or empyema.



Ultrasound of right lung base showing fluid as an echo free space



Ultrasound showing heavy loculation

2) Aetiological diagnosis

The history, examination and investigations all play a role in arriving at an aetiological diagnosis of a pleural effusion.

- **History**

The history should be specifically directed at identifying:

a) conditions associated with fluid retention such as congestive heart failure, nephrotic syndrome and cirrhosis.

b) malignancies, especially of lung, breast, ovary, stomach and lymphoma.

c) collagen vascular disease such as SLE and rheumatoid arthritis.

- **Examination**

In the physical examination, signs of the above mentioned diseases should be sought. Thus it is important to look for dependent oedema, pallor, lymphadenopathy, clubbing and features of connective tissue disorders in the general examination. The cardiovascular system should be examined for elevated jugular venous pressure, cardiomegaly and the third heart sound of heart failure. A thorough examination of the respiratory system is necessary to identify a consolidation or malignancy. Hepatosplenomegaly and ascites should be looked for in the abdominal examination.

- **Investigations**

Basic investigations as well as specialised investigations are necessary for the diagnosis of the aetiology of a pleural effusion. (Table 5)

Table 5. Investigations in the aetiological diagnosis of a pleural effusion

1. Chest radiograph
2. WBC/DC
3. ESR, CRP
4. Mantoux test
5. ANF
6. Rheumatoid factor
7. Diagnostic thoracentesis
8. Pleural biopsy
9. Thoracoscopy
10. Thoracotomy
11. Autopsy

1. Chest radiograph

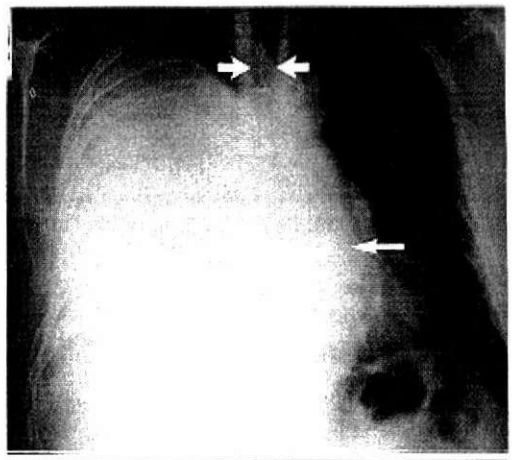
Evidence of lung infection, primary bronchial carcinoma, metastatic lung disease, heart failure and rheumatoid lung are revealed by the chest x ray. Other factors that need to be appreciated in the chest x ray include, the size of the effusion, whether the effusion is unilateral or bilateral, whether the heart size is normal and the lack of mediastinal shift in the presence of a massive pleural effusion.

A normal heart with bilateral pleural effusions can be seen in malignancy (50%), SLE, hypoalbuminaemia, constrictive pericarditis, rheumatoid pleurisy, benign asbestos pleural effusion and cirrhosis.

The absence of a mediastinal shift in the face of a large effusion almost always indicates malignancy[3]. It could be due to carcinoma of the ipsilateral main stem bronchus resulting in atelectasis, a fixed mediastinum due to malignant lymph nodes or conditions mimicking a large effusion such as malignant mesothelioma or extensive tumour infiltration.

2. CT and MRI

CT and MRI scanning of the thorax give more detailed morphological information than the chest x ray. They also provide clues to the possible nature and cause of the effusion; eg: thickening of the parietal pleura and chest wall involvement in exudates. However, CT and MRI scanning do not obviate the need for thoracocentesis or other invasive diagnostic procedures[3].



Large right sided pleural effusion without any mediastinal shift

3. Diagnostic thoracentesis

This investigation is a must, unless there is evidence of obvious fluid retention (eg: congestive heart failure, nephrotic syndrome, cirrhosis) or the effusion is clinically insignificant (<10 mm thick on ultrasonography or lateral decubitus radiography). Even in the presence of fluid retention, thoracentesis is indicated if fever or chest pain is present or the effusions are asymmetric. Pleural effusions due to heart failure usually resolve with adequate diuretic therapy within 3 days;[4] Hence thoracentesis is again indicated if effusions persist beyond 3 days.

A conventional site for the aspiration is posteriorly, about 10 cm lateral to the spine and one intercostal space below the upper level of fluid detected by percussion. The site for aspiration is better determined with the help of chest radiograph. Ultrasound guidance is necessary if there are difficulties in obtaining fluid or the effusion is small or loculated[5]. If the fluid is loculated, the aspiration should be done over the appropriate site. 50-100 ml of fluid should be aspirated and sent for investigations.

If the patient has shortness of breath at rest, a therapeutic thoracentesis is indicated and up to 1500 ml of fluid can be removed.

Routine chest radiography following thoracentesis is not necessary. It is indicated if air is aspirated or the patient develops cough, dyspnoea or chest pain. Loss of tactile vocal fremitus over the upper part of the aspirated chest is another indication[6,7].

- **Pleural fluid analysis**

Pleural fluid analysis reveals much information about the cause of the effusion.

Odour	–	A putrid odour indicates infection due to anaerobes
Macroscopy	–	Serous, turbid, purulent, blood stained or chylous effusion
Biochemistry	–	Protein, LDH, glucose, amylase, pH, cholesterol
Microbiology	–	Pleural fluid culture and ABST and staining for Acid Fast Bacilli
Immunology	–	PCR for M. tuberculosis
Cytology	–	Any increase in normal cells (polymorphs, mononuclear cells, lymphocytes) and the presence of abnormal cells (malignant cells)
Others	–	Other investigations are carried out when appropriate. (eg: haematocrit)

Tests indicated according to the appearance of pleural fluid[1]

Appearance of fluid	Tests indicated	Interpretation of results
Bloody	Haematocrit (Pleural fluid to Blood ratio)	<1% – Insignificant 1-20% – Blood stained effusion – cancer, trauma, Pul.embolus >50% – Haemothorax
Cloudy or turbid*	Centrifugation	Clear supernatant – empyema Turbid supernatant – chylothorax or pseudochylothorax
Turbid supernatant	Triglyceride level	>110 mg% – chylothorax 50-110 mg% – do a lipoprotein analysis – if chylomicrons are present – chylothorax <50 mg% – do cholesterol – if >250mg% – psedochylothorax

*Cloudy appearance is consistent with the presence of either cells, debris or high lipid levels

Blood stained pleural effusions[1,8]

As little as 1 ml of blood in 500 ml of pleural fluid can give rise to blood staining. So it is important to find out if it is a haemothorax or a blood stained pleural effusion. Pleural fluid to blood haematocrit ratio is helpful in differentiating between these two conditions, where the ratio is >50% in haemothorax and 1-20% in blood stained pleural effusions. A haematocrit of <1% is insignificant.

A haemothorax could be caused by trauma, pneumothorax, dissecting aneurysm, bleeding disorders, anticoagulants and pleural endometriosis. A blood stained pleural effusion may be found in pulmonary infarction, malignancy and trauma.

Chylothorax and pseudochylothorax[9]

In a chylothorax, the fluid is thick, opalescent, whitish (milky) or the colour of chocolate milk. However, an empyema can give rise to a similar appearance. Centrifugation of fluid can differentiate between these two conditions, where an empyema shows a clear supernatant and a chylothorax shows three layers. The pleural fluid triglyceride level in chylothorax is > 110mg%.

Pseudochylothorax is not associated with chyle or lymphatics. It occurs when fluid has been present in the pleural space for a long time. The pleural fluid triglyceride level is <110mg% although cholesterol level in pseudochylpthorax is > 200 mg%.

Exudate or transudate?

All the bloody effusions with a pleural fluid to blood haematocrit ratio > 1% and all the purulent and chylous effusions are exudates. Serous (straw coloured) effusions can be either exudates or transudates.

For the past several decades, transudates have been differentiated from exudates according to Light's criteria[10,11]. A serous effusion is considered an exudate if one of the following three conditions is met.

i. Pleural fluid to serum protein ration >0.5

ii. Pleural fluid to serum LDH > 0.6

iii. Pleural fluid LDH value > 2/3rd the upper normal level of serum LDH.

Light's criteria are the most sensitive for identifying exudates but have lower specificity than other criteria[12].

If a transudative effusion is clinically suggested but the pleural fluid is an exudate according to Light's criteria, the serum-pleural fluid albumin gradient should be determined. A gradient of >1.2 g/dL indicates a transudative effusion[13].

Sensitivity of tests to distinguish exudative from transudative effusions[12,13]

Test	Sensitivity%	Specificity%
Light's criteria (>2)	98	83
Ratio of pleural fluid protein to serum protein >0.5	86	84
Ratio of pleural fluid LDH to serum LDH >0.6	90	82
Pleural fluid LDH > 2/3rds the upper limit of normal for serum	82	89
Pleural fluid cholesterol >60 mg/dL	54	93
Pleural fluid cholesterol >43 mg/dL	75	80
Ratio of pleural fluid cholesterol to serum cholesterol >0.3	89	81
Serum – pleural fluid albumin gradient <1.2 g/dL	87	92

For an effusion that is likely to be transudative, one should only do pleural fluid proteins and lactate dehydrogenase levels. Further tests provide no additional information and sometimes produce misleading results[14].

Some diseases may appear in some patients as transudates and others as exudates; eg: myxoedema, pulmonary infarction.

Additional tests are needed in exudative effusions. These include total and differential cell counts, smears and cultures for organisms, measurement of glucose, lactate dehydrogenase and amylase levels, cytologic analysis and testing for pleural fluid markers of tuberculosis.

Total and differential cell counts

Increase in pleural fluid neutrophils is seen in pyogenic infections and acute pancreatitis. An elevated mononuclear cell count may be due to mesothelial cells, macrophages, plasma cells, lymphocytes or malignant cells. Lymphocytes are increased in tuberculosis, lymphoma and malignancy. Malignant cells may be detected in a pleural based malignancy[15].

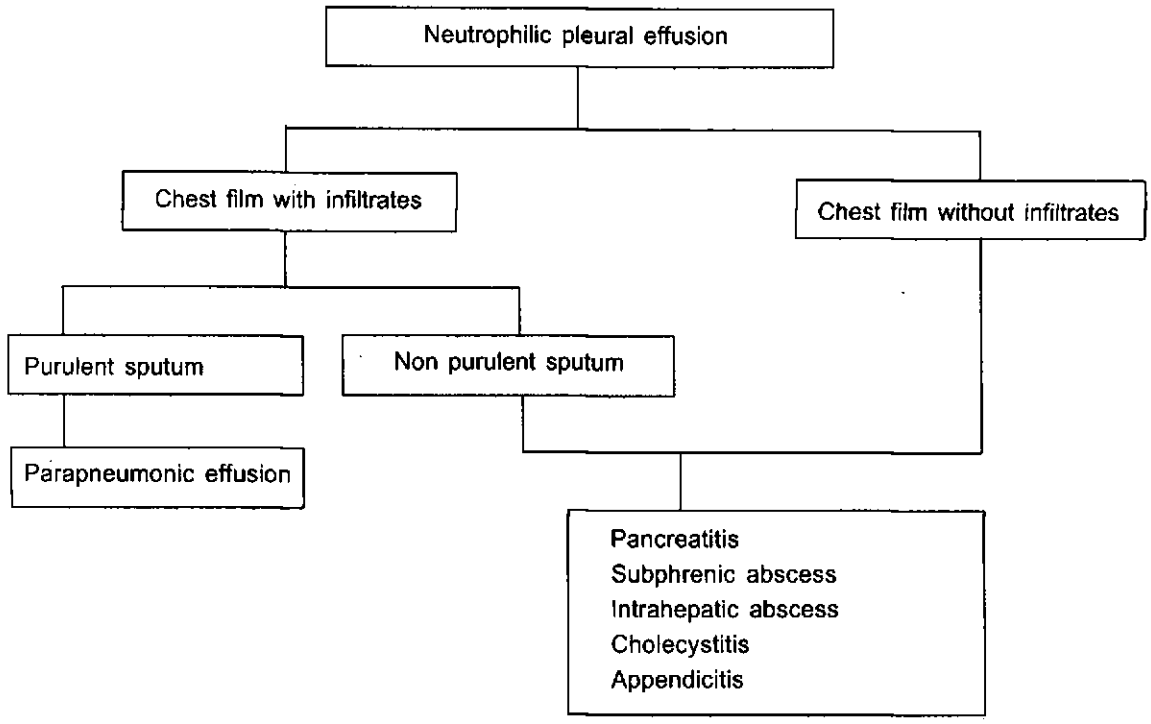
A ***predominantly neutrophilic (>50%) pleural effusion*** suggests an acute process involving the pleura and may be parapneumonic or secondary to subdiaphragmatic infections; eg: liver abscess, cholecystitis, appendicitis, perforated peptic ulcer, diverticulitis, acute pancreatitis[16]. (Fig 1)

A predominantly mononuclear (>50%) pleural effusion indicates a chronic process.

Mononuclear cells (lymphocytes [large & small], macrophages, mesothelial cells, malignant cells) are seen in effusions associated with viral infection, tuberculosis, malignancy, pulmonary embolism and rare causes such as Dressler's syndrome, asbestosis, SLE, drugs, fungal and parasitic infections. However, not all laboratories differentiate small lymphocytes from other mononuclear cells.

Small lymphocytic pleural effusions are found in malignancy, tuberculosis and after coronary artery by-pass surgery[16,17,18]. In malignancy, the number of nucleated cells is modest (1500-4000/microL) and 50 -70% of these cells are lymphocytes. The red cell count in malignancy is 30000-50000/microL. In tuberculosis, over 90% of the cells are lymphocytes.

Figure 1. Neutrophilic pleural effusions



Pleural fluid eosinophilia (>10% eosinophils) is caused in about 2/3rds of cases by blood or air in the pleural space[19]. Unusual causes of pleural fluid eosinophilia include reaction to drugs (dantrolene, bromocriptine, nitrofurantoin), exposure to asbestos, paragonimiasis, and Churge-Strauss syndrome[20].

Smears and cultures

Gram's staining and culture for both aerobic and anaerobic bacteria will identify infected pleural fluid. If blood culture bottles are used and inoculated at the bedside, the yield is increased[21]. If there is a predominance of lymphocytes, cultures for mycobacteria and fungi are indicated. Smears are rarely positive for mycobacteria in the absence of AIDS; However smears may reveal fungi[22,23].

Pleural fluid tests for malignancies

Malignant pleural effusions

These are most commonly found in carcinoma of lung (36%) and breast (25%). Other causes of malignant effusions include lymphoma (10%), carcinoma of ovary or stomach and carcinoma with unknown primary[3].

Malignant effusions can only be diagnosed by demonstrating malignant cells in the pleural fluid or pleural tissue. Cytology is more sensitive than percutaneous pleural biopsy in detecting malignancy. If the first thoracentesis is negative for malignant cells, repeat the test after a few days. This will provide pleural fluid with fewer mesothelial cells and freshly exfoliated malignant cells. Sensitivity of cytology in detecting different types of pleural malignancies is as follows. Metastatic adenocarcinoma 70%, mesothelioma 10%, squamous cell carcinoma 20%, lymphoma 25-50%, sarcoma 25%[1,16,24].

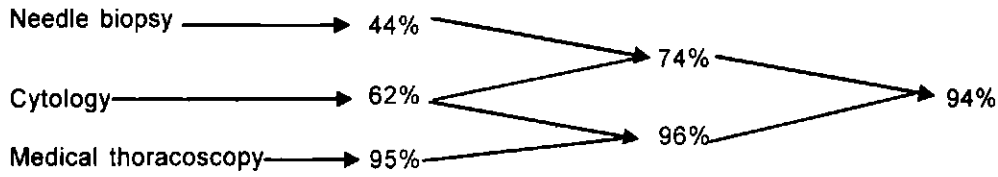
If the cytology is negative for malignant cells medical thoracoscopy and biopsy is the procedure of choice. As this procedure is not yet available in Sri Lanka, a percutaneous pleural biopsy should be carried out. However, chest wall pleura is not involved in 30% of cases. If the diagnosis is inconclusive, an open pleural biopsy may have to be carried out. (Fig 2)

If a lymphoma is suspected, flow cytometry can demonstrate presence of a clonal population confirming the diagnosis[22]. Measurement of tumour markers in the pleural fluid has proved disappointing in establishing the diagnosis of pleural cancer[26].

Tuberculous pleural effusion[22,27]

This should be the first diagnosis suspected in a lymphocytic pleural effusion in a young person. A definite diagnosis can be achieved only when Mycobacterium tuberculosis is demonstrated in pleural fluid or sputum specimens or when caseous granulomata are found in pleural biopsies.

Figure 2. Sensitivity of different techniques used in the diagnosis of malignant pleural effusions[3]



❑ *Tuberculin skin test*

A positive tuberculin skin test in a patient with a pleural exudate, strongly suggests the diagnosis of tuberculosis in a population with a high prevalence of tuberculosis. A negative test however, does not rule out tuberculosis, as it may be found in 30% of immunocompetent and up to 59% of HIV infected patients with tuberculosis.

The sensitivity of different tests in the diagnosis of tuberculous effusions varies from 10% 98%. (eg: pleural fluid culture 10-35%, needle pleural biopsy culture 39-65%, needle pleural biopsy histology 56-82%, combined histology and culture 86%, thoracoscopy 98%).

❑ *New diagnostic parameters*

Several new diagnostic tests have been developed for the diagnosis of tuberculous effusions. These have become necessary as the older diagnostic investigations were less sensitive or required a long time to yield results. (eg; Needle biopsy is not conclusive in 20-40%. Culture of M. tuberculosis takes 33 days, although radiometric mycobacterial culture system – BACTEC – can give results in 18 days).

The following tests are being increasingly utilised in the diagnosis of tuberculous effusions.

i. Adenosine deaminase (ADA)[28,29]
ii. Interferon gamma (IFN)30
iii. Polymerase Chain Reaction (PCR)

Adenosine deaminase (ADA)[28,29]

This enzyme catalyses the conversion of adenosine and deoxyadenosine to inosine and deoxy inosine. Tuberculous effusions contain a higher level of ADA than most other exudates. ADA 2 is found in tuberculosis while ADA 1 is seen in parapneumonic effusions. The usefulness of ADA as a diagnostic test depends on the prevalence of tuberculosis. In populations with a high prevalence of tuberculosis, its sensitivity is 95% and the specificity is 90%.

Polymerase Chain Reaction (PCR)

The sensitivity of PCR varies from 20-81%. However, the sensitivity in culture positive cases is 100%. The specificity of this test is 78-100%.

Pleural fluid glucose level

A pleural fluid glucose concentration of < 50mg/dL is associated with pyogenic effusions[31] (complicated parapneumonic effusions, sub-diaphragmatic infection)[32,33] and malignancy. Less common causes are haemothorax, tuberculosis, rheumatoid pleurisy. Rarely Churge-Strauss syndrome, lupus pleuritis and paragonimiasis can cause low sugar levels in pleural fluid.

Pleural fluid amylase level

An increase in pleural fluid amylase is found in acute pancreatitis and oesophageal perforation. Amylase should be measured only if these conditions are clinically suspected[34].

Pleural fluid LDH level

This correlates well with the degree of pleural inflammation. A LDH level that increases with repeated thoracentesis indicates an increasing degree of inflammation and vice-versa. In the presence of an increasing LDH, a diagnosis should be aggressively pursued.

Measurement of pleural fluid pH

This is indicated in the presence of parapneumonic and malignant effusions. A pleural pH of <7.2 in a patient with a parapneumonic effusion indicates intense bacterial activity and the need for tube thoracostomy[35,36]. A pH in this range in a patient with a malignant effusion indicates that the patient's life expectancy is about 30 days and that chemical pleurodesis is likely to fail[1]. The markedly abnormal pleura (due to large tumour burden and fibrosis) interferes with glucose transport from blood to pleural fluid leading to low glucose levels. Glucose that enters is metabolized in to CO_2 and lactate. The abnormal pleura prevents efflux of these products resulting in pleural fluid acidosis[3].

Immunologic tests on pleural fluid

Determination of antinuclear antibody (ANA) titres, rheumatoid factor (RF) levels or demonstration of "LE cells" add little diagnostic information. These disorders are diagnosed by the clinical picture and appropriate serology[37].

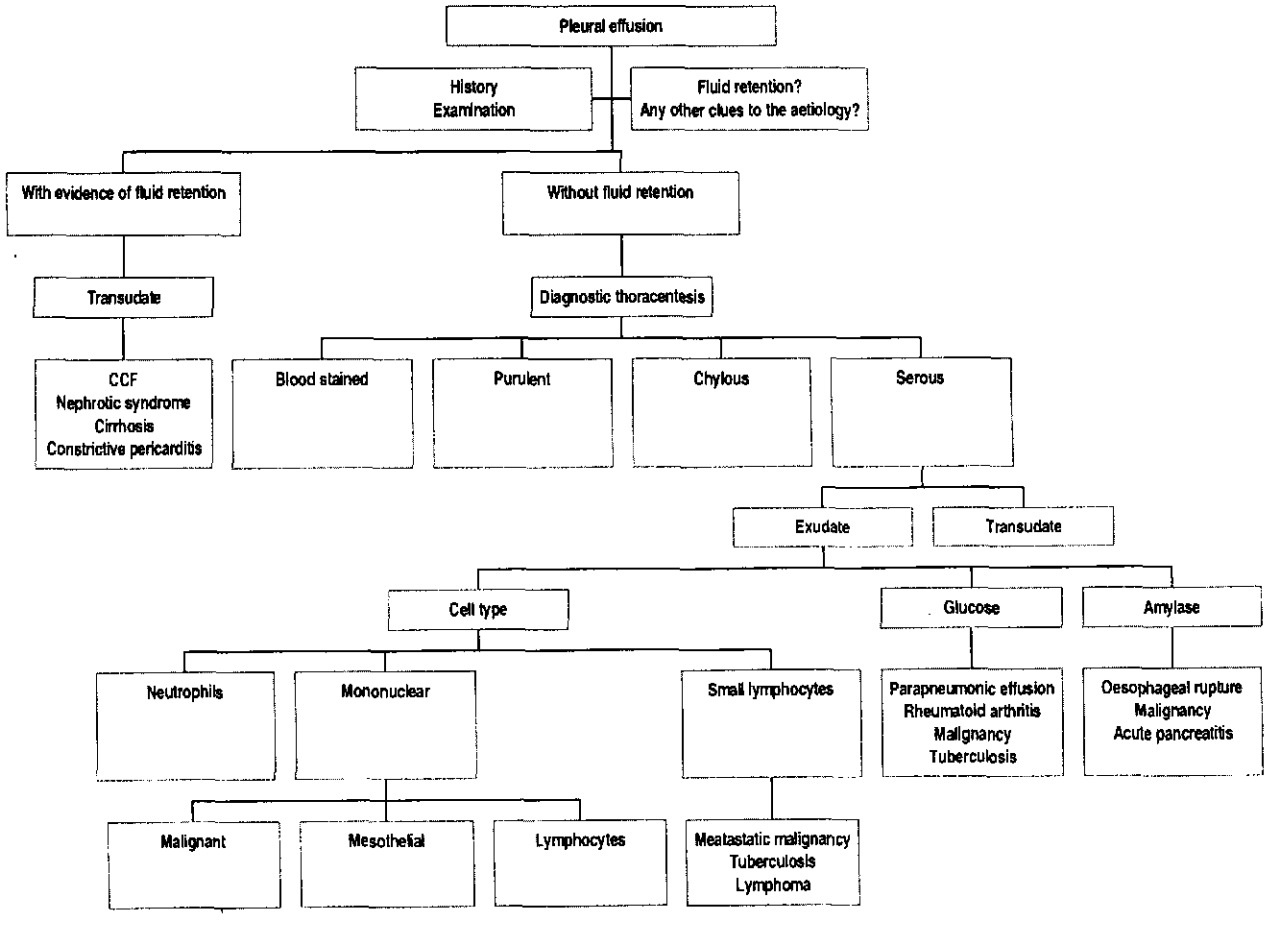
Evaluation for pulmonary embolism

In the presence of classical clinical picture (pleuritic chest pain, haemoptysis and/or dyspnoea out of proportion to the size of the effusion), the best screening test is the measurement of D-dimer levels in peripheral blood[38]. If a sensitive test is used and it is negative, pulmonary embolism is essentially ruled out. In positive cases confirmatory testing is required.

Summary

Pleural effusions are a common finding. When a pleural effusion is suspected, it is necessary to confirm its presence as well as detect its aetiology. Physical examination usually reveals moderate to large effusions, which can be confirmed with chest radiography or ultrasonography. Diagnostic thoracentesis should be performed in all cases unless the effusion is very small (<10 mm in the decubitus film) or there is evidence of obvious fluid retention and the effusions are symmetrical. Ultrasound guidance is indicated if the effusion is small or difficulty is encountered in obtaining fluid. Analysis of pleural fluid is invaluable in the aetiological diagnosis of a pleural effusion. A systematic approach to analysis of the fluid in conjunction with the clinical presentation should allow the clinician to diagnose the cause of an effusion in 75% of patient in the first encounter. If the fluid is likely to be a transudate from the clinical picture, what is required are the protein and the LDH levels in pleural fluid. If the patient has an exudative pleural effusion according to Light's criteria, (the pleural fluid should be stained with gram's stain and cultured for bacteria) the following additional tests are indicated; pleural fluid, total and differential cell counts, glucose level, gram's stain and culture, pleural fluid markers of tuberculosis and cytologic analysis. Pleural fluid pH is indicated for parapneumonic and malignant effusions. If pancreatitis or ruptured oesophagus is suspected, pleural fluid amylase should be measured. No diagnosis is ever established in about 15% of patients despite invasive procedures such as thoracoscopy or open pleural biopsy[39].

Figure 3. Diagnostic evaluation of a pleural effusion.



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Questions

Question 1

A 35-year-old man is evaluated because of a 2 week history of low grade fevers, fatigue, cough, pleuritic chest pain, and increasing dyspnoea on exertion. He is a construction worker and is having difficulty performing his usual tasks. He has a 10 pack year history of cigarette smoking. On physical examination, he has right chest pain but no respiratory distress at rest. Temperature is 38.2 'C (100.8 'F), pulse rate is 112/min and regular, and respiration rate is 20/min. There is evidence of a right pleural effusion and no other abnormalities.

Peripheral blood leukocyte count is 9,000/microL, with 80% neutrophils and 15% lymphocytes. Liver function test results are normal. Chest radiograph shows a moderate right pleural effusion with minimal contralateral shift and no parenchymal infiltrates.

Thoracentesis yields; minimally turbid yellow fluid with results as follows.

Pleural fluid nucleated cell count	3000/μL with 5% neutrophils, 85% lymphocytes and 1% macrophages
Pleural fluid total protein	5.2 g/dL
Pleural fluid serum lactate dehydrogenase	230 U/L
Pleural fluid glucose	80 mg/dL
Pleural fluid pH	7.36

Pleural fluid Gram and acid fast bacilli stains are negative. Tuberculin skin test is negative. Cytologic evaluation for malignant cells is negative.

What is the most likely diagnosis?

(A) Tuberculous pleurisy
(B) Lung cancer
(C) Parapneumonic effusion
(D) Pulmonary embolism
(E) Benign asbestos pleural effusion

Question 2

A 60 year old man is evaluated because of a 6 week history of progressive dyspnoea on exertion, fatigue, a decrease in appetite, and a weight loss of 1.8 kg (4 lb). He has a 30 pack year history of cigarette smoking and drinks two or three cocktails every evening. He has no gastrointestinal complaints and no history of a febrile illness.

On physical examination, he is afebrile with normal vital signs. The only abnormalities noted on chest examination are findings compatible with a right pleural effusion. Chest radiograph confirms a pleural effusion occupying 40% of the right hemithorax without evidence of loculation. There are no obvious parenchymal lesions and no mediastinal adenopathy.

Results of pleural fluid analysis are as follows.

Pleural fluid nucleated cell count	2800/μpL with 10% neutrophils, 50% lymphocytes, 30% macrophages and 10% mesothelial cells
Pleural fluid total protein	3.8 g /dL (pleural fluid/serum ratio 0.60)
Pleural fluid serum lactate dehydrogenase	2 10 1U/L (ratio of pleural fluid to upper limits of normal serum lactate dehydrogenase 0.72)
Pleural fluid amylase	30 mg/dL (pleural fluid/serum ratio 0.5)
Pleural fluid glucose	50 mg/dL
Pleural fluid pH	7.26

Which of the following is the most likely diagnosis?

(A) Complicated parapneumonic effusion
(B) Esophageal rupture
(C) Rheumatoid pleurisy
(D) Acute pancreatitis
(E) Malignant effusion