INTRODUCTION:
Pleural effusions occur as a result of increased fluid formation and/or reduced fluid reabsorption. The precise pathophysiology of fluid accumulation varies according to underlying pathologies. As the Differential diagnosis for a pleural effusion is wide, a systematic approach to investigation is necessary. The objective is to establish an early diagnosis and facilitating treatment with minimum invasive intervention. More than 50 local and systemic causes of pleural effusion have been recognized.
The appropriate clinical history and physical examination of a patient with a pleural effusion may guide the clinician as to whether the effusion is a transudate or an exudate. For bilateral effusions in a clinical setting strongly suggestive of a transudate like cardiac failure, chronic liver disease or nephritic syndrome aspiration of fluid may not be carried out unless there are atypical features or they fail to respond to standard treatment.
Tests on the pleural fluid analysis are usually not helpful in diagnosing pulmonary embolism. Such effusions are usually small in volume and dyspnea is often out of proportion to the size of the effusion. Most of these patients will have pleuritic chest pain as well. Drug history is also important. Although uncommon, a number of medications have been reported to cause exudative pleural effusions which include; Methotrexate, Amiodarone, Phenytoin, Nitrofurantoin and B-blockers. An occupational history including details about known or suspected asbestos exposure and potential Secondary exposure via family member should be noted.

INITIAL DIAGNOSTIC WORKUP:

Plain Chest radiography:
The plain chest radiographic features of pleural effusion are usually characteristic. The posteroanterior (PA) chest x-ray is abnormal in the presence of about 200 ml of pleural fluid. However, only 50 ml of pleural fluid can produce detectable posterior costophrenic angle blunting on a lateral chest X-Ray. In critical patients, most chest X-Rays are performed as AP supine position with free pleural fluid moving posteriorly in the dependent portion of the chest. Consequently, effusions are seen as an increase in hemithorax opacity. Other signs include the loss of the sharp silhouette of the ipsilateral hemidiaphragm and fluid tracking down into the oblique or horizontal fissures resulting in apparent fissure thickening. The volume of pleural fluid is commonly underestimated on a supine chest X-Ray and 'normal' appearances do not exclude the presence of an effusion. Subpulmonic effusions occur when pleural fluid accumulates between the diaphragmatic surface of the lung and the diaphragm. They are often transudates, can be difficult to diagnose on the PA film and may require an ultrasound scan. The PA film will often show a lateral peaking of an apparently raised hemidiaphragm which has a steep lateral slope with a gradual medial slope. The lateral x-ray may have a flat appearance of the posterior aspect of the hemidiaphragm with a steep downward slope at the major fissure.
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**Ultrasound:**
Bedside ultrasound guided aspiration significantly increases the chances of successful tap while reducing the risk of organ puncture. Ultrasound detects pleural fluid septations with greater sensitivity than CT. Studies have shown that fluid can be successfully obtained using ultrasound in up to 88% of patients after a failed clinical and plain chest X-Ray-guided attempt. Ultrasound guidance reduces the incidence of iatrogenic pneumothorax following thoracentesis. All these benefits appear to be reduced when fluid is aspirated on bedside after getting the “aspiration site marked” in radiology departments, presumably due to differences in patient positioning between the ultrasound and the procedure. Puncture of liver, spleen and lungs have occurred even in large effusions.

**Diagnostic algorithm for the investigation of a pleural effusion**

1. **History, clinical examination & CXR**
   - Does the clinical picture suggest a transudate?
     - e.g. LVF, hypoalbuminaemia, dialysis
     - ↓
   - Is it a transudate? Treat likely cause
     - ↓
   - Resolved? YES, STOP further; No Cause found:
     - ↓
   - Re-consider treatable conditions such as PE, TB, chronic heart failure and lymphoma.
     - (Keep under observation).
     - ↓
   - Has the fluid analysis and clinical features given a diagnosis? No;
     - Refer to a chest physician
     - ↓

2. **Pleural aspiration (with ultrasound guidance)**
   - Send for: cytology, protein, LDH, pH Gram stain, culture and sensitivity
   - ↓
   - Cause found, ---- Treat appropriately
     - Request CT thorax with contrast.
     - ↓
   - Consider LA thoracoscopy or surgical VATS/ Consider radiological guided pleural biopsy +/- chest tube drainage if symptomatic
Ultrasound is superior to plain radiography in diagnosing and quantifying pleural effusions and distinguishes pleural fluid from thickening with high specificity, particularly when color Doppler is employed. Ultrasound detects septations within pleural fluid with greater sensitivity than CT scanning. A septated appearance may be observed in malignant effusions or pleural infection and occurs with similar frequency in the two diagnoses. Ultrasound positively identifies exudative effusions when pleural fluid is complex, septated or echogenic, although simple (anechoic) effusions can be exudates or transudates. Ultrasound features can distinguish malignant from benign effusions. Qureshi et al demonstrated 95% specificity for a malignant diagnosis, 95% for parietal pleural thickening >1 cm, 100% for visceral pleural thickening, 95% for diaphragmatic thickening >7 mm and 100% for diaphragmatic nodules as visualized on ultrasound examination.

**PLEURAL FLUID ASPIRATION:**
A diagnostic pleural fluid sample should be aspirated with a fine-bore (21G) needle and a 50 ml syringe. Bedside ultrasound guidance is recommended as it improves the success rate and reduces complications. Pleural fluid should always be sent for protein, lactate dehydrogenase, Gram stain, cytology and microbiological culture. These preliminary tests are used to guide further investigation. A lateral site for aspiration is preferred, provided that adequate fluid is demonstrated here on ultrasound. The risk of intercostal vessel trauma increases with more posterior or medial punctures. If there is diagnostic suspicion of pleural infection and a pleural fluid pH is to be measured, aspirated fluid should immediately be drawn into a heparinized blood gas syringe which should then be capped while awaiting analysis to avoid exposure of the fluid to the air. The remaining sample should be sent for microbiological (5 ml), biochemical (2-5 ml) and cytological (remaining sample which should be 20-40 ml) analysis. Microscopic examination of Gram stained pleural fluid sediment is necessary for all pleural fluid samples. If infection is suspected, some of the pleural fluid should be sent in blood culture bottles which increases diagnostic accuracy, particularly for anaerobic organisms.

There is conflicting evidence regarding the optimum volume of pleural fluid for diagnosis of malignancy; sensitivity depends on the cellularity of the sample and processing technique as well as volume submitted. It is sensible to send as large a volume as possible from the 50-60 ml sample obtained following diagnostic aspiration as other tests only require small volumes. At room temperature the sample for cytology should be sent to the laboratory as quickly as possible but, if a delay is anticipated, the specimen can be refrigerated at 4-8 °C for up to 14 days with no deterioration in the diagnostic yield for malignancy.

**Appearance:**
The appearance of the pleural fluid and any odor should be recorded. A pleural fluid haematocrit is helpful in the diagnosis of hemothorax. Fluid may appear serous, blood-tinged, frankly bloody or purulent. Centrifuging turbid or milky pleural fluid will distinguish between empyema and lipid effusions. If the supernatant is clear, the turbid fluid was due to cell debris and empyema is likely while, if it is still turbid, chylothorax or pseudochylothorax are likely. The unpleasant smell of anaerobic infection may guide antibiotic choices and the smell of ammonia suggests urinothorax. Grossly bloody pleural fluid is usually due to malignancy, pulmonary embolus with infarction, Tuberculosis, trauma, benign asbestos pleural effusions or post-cardiac injury syndrome.

Differentiating between a pleural fluid exudate and transudate:
Light’s criteria should be used to distinguish between a pleural fluid is exudate or transudate the total protein and lactate dehydrogenase (LDH) should be measured in both blood and pleural fluid. Categorization of pleural effusions into transudates and exudates is an important early step in narrowing the differential diagnosis and directing subsequent investigations and management. Classically, pleural fluid protein >30 g/l has indicated an exudate and <30 g/l a transudate. This classification is not accurate when serum protein is abnormal or when the pleural fluid protein is close to 30g/l and, as this is very common, the application of Light’s criteria is always recommended.

SAMPLE COLLECTION GUIDANCE:
Biochemistry:
LDH and protein 25ml in plain container or serum blood collection tube depending on local policy. Blood should be sent simultaneously to biochemistry for total protein and LDH so that Light’s criteria can be applied.

Microscopy and culture (MC and S):
5 ml in plain container. If pleural infection is particularly suspected, a further 5 ml in both anaerobic and aerobic blood culture bottles should be sent Cytological examination and 36. differential cell count. Maximum volume from remaining available sample in a plain universal container. Refrigerate if delay in processing anticipated (eg, out of hours)

Tests sent only in selected cases:
PH In non-purulent effusions when pleural infection is suspected. 0.5-1 ml drawn up into a heparinized blood gas syringe immediately after aspiration. The syringe should be capped to avoid exposure to air. Glucose Occasionally useful in diagnosis of rheumatoid effusion. 1-2 ml in fluoride oxalate tube sent to biochemistry. Acid-fast bacilli and TB culture 5 ml sample in plain Container when there is clinical suspicion of TB pleuritis. Request for AFB C&S besides smear.. Triglycerides and cholesterol to distinguish chylothorax from pseudochylothorax in milky effusions. Can usually be requested with routine biochemistry (LDH, protein) using the same sample. Amylase occasionally useful in suspected pancreatitis-related effusion. Can usually be requested with routine biochemistry. Haematocrit for diagnosing hemothorax. 1-2 ml sample in EDTA container sent to hematology (LDH, lactate dehydrogenase; PH, pulmonary hypertension; TB, tuberculosis)
BTS guidelines

In congestive cardiac failure, diuretic therapy increases the concentration of protein, lactate dehydrogenase (LDH) and lipids in pleural fluid and, in this context, Light’s criteria are likely to misdiagnose a significant proportion of effusions as exudates. It is more appropriate to make a likely diagnosis of transudate or exudates in view of clinical judgment when pleural protein and LDH levels are close to cut-off values.

N-terminal pro-brain natriuretic peptide (NT-proBNP):

NT-proBNP is a sensitive marker of both systolic and diastolic cardiac failure. Levels in blood and pleural fluid correlate closely and measurement in blood is sufficient in discriminating transudates associated with congestive heart failure from other transudative or exudative causes; cut-off value varies from 600 to 4000 pg/ml (with 1500 pg/ml being most commonly used). NT-proBNP has been shown to correctly diagnose congestive heart failure as a cause of most effusions that have been misclassified as exudates by Light’s criteria. Use of this test may therefore avoid repeated invasive investigations in patients where there is a strong clinical suspicion of cardiac failure. Evidence for the use of measuring BNP (also known as C-terminal BNP, the active peptide from which NT-proBNP is cleaved) is relatively scarce to date.

Pleural fluid differential cell counts:

Pleural fluid differential cell counts are helpful in narrowing the differential diagnosis but none are disease specific. Any long-standing pleural effusion tends to become lymphocytic.
If the pleural fluid differential cell count shows a predominant lymphocytosis (>50% cells are lymphocytes), the most likely diagnoses worldwide are malignancy and tuberculosis (TB). Cardiac failure, cirrhosis and other causes of transudates would also have lymphocyte predominance being chronic conditions. Very high lymphocyte proportions (>80%) occur most frequently in TB, lymphoma, chronic rheumatoid pleurisy, Sarcoidosis and late post-coronary artery bypass grafting (CABG) effusions. Neutrophil-predominant pleural effusions are associated with acute processes like in parapneumonic effusions, pulmonary embolism, acute TB and benign asbestos pleural effusions. Pleural effusions in which >10% of cells are eosinophils are defined as eosinophilic; most common cause of which is air or blood in the pleural space. It can also occur in parapneumonic effusions, drug-induced pleurisy, benign asbestos pleural effusions, Churg-Strauss syndrome, lymphoma, pulmonary infarction and parasitic disease.

**pH:**
In non-purulent effusions, when infection is suspected, pleural fluid pH should be measured. In a parapneumonic effusion, a pH of <7.20 indicates the need for intercostal tube drainage. Pleural fluid acidosis (pH <7.30) occurs in malignant effusions, complicated pleural infection, connective tissue diseases (particularly rheumatoid arthritis), TB and esophageal rupture. In isolation, it does not distinguish between these causes. Pleural fluid acidosis reflects an increase in lactic acid and carbon dioxide production. Increased consumption of glucose without replacement in the same conditions means that pleural fluid often has both a low pH and low glucose concentration. Pleural fluid should be collected and transported without exposure to atmospheric air and local anaesthetic should be avoided for diagnostic aspirations where the pH will be used to guide management. Pleural pH does not change significantly if processing is delayed for up to an hour at room temperature. An arterial blood gas analyser should be used.

**Glucose:**
In the absence of pleural pathology, glucose diffuses freely across the pleural membrane and the pleural fluid glucose concentration is equivalent to blood. A low pleural fluid glucose level (<3.4 mmol/l) may be found in complicated parapneumonic effusions, empyema, rheumatoid pleuritis and pleural effusions associated with TB, malignancy and esophageal rupture. The most common causes of a very low pleural fluid glucose level (<1.6 mmol/l) are rheumatoid arthritis and empyema. Although glucose is usually low in pleural infection and correlates with pleural fluid pH values, it is a significantly less accurate indicator for chest tube drainage than pH.

**Amylase:**
Pleural effusion occurs in more than 50% of cases of acute pancreatitis. Pleural fluid amylase levels are termed elevated if they are higher than the upper limit of normal for serum or the pleural fluid/serum ratio is >1.0.18 This suggests acute pancreatitis, pancreatic pseudo cyst, rupture of the esophagus, ruptured ectopic pregnancy or pleural malignancy (especially adenocarcinoma). Routine measurements of pleural fluid amylase or its iso enzymes are not warranted. Patients with acute pancreatitis and a pleural effusion tend to have more severe
disease and a higher likelihood of subsequently developing a pseudo cyst than those without effusions. If esophageal rupture is entertained as a differential diagnosis, urgent more specific investigation by contrast radiography or endoscopy is indicated.

**CYTOLOGY:**

If malignancy is suspected, cytological examination of the pleural fluid is a quick and minimally invasive way to obtain a diagnosis\(^\text{20}\). Sending more than two specimens of pleural fluid taken on different occasions is not required. The diagnostic yield for malignancy depends on sample preparation, the experience of the cytologist and on tumor type.

The diagnostic rate is higher for adenocarcinoma than for mesothelioma, squamous cell carcinoma, lymphoma and sarcoma. As much fluid as possible should be sent for cytology from the available diagnostic sample. When the initial result is negative but malignancy is suspected, then sending of a larger volume sample following a second aspiration should be considered.

Pleural fluid should be sent in a plain container which allows the cellular portion to separate, forming a fibrinous ‘clot’ containing more malignant cells. These can then undergo histological examination and are reported with the fluid cytology. To keep the cells in free suspension fluid may be sent in bottles containing sodium citrate.

The yield for malignancy increases if both cell blocks and smears are prepared from centrifuged pleural fluid. Once malignancy has been confirmed morphologically, immunocytochemistry should be used to differentiate between different malignant cell types.

**TUMOR MARKERS:**

For a definite diagnosis a panel of pleural fluid tumor markers including CEA, CA-125, CA 15-3 and CYFRA has been shown to reach a combined sensitivity of only 54%. Thus negative results do not help in investigation or monitoring. Mesothelin is a glycoprotein tumor marker that is present at higher mean concentrations in the blood and pleural fluid of patients with malignant mesothelioma than in patients with other causes of pleural effusion\(^\text{21}\). Positive results have also been recognized in bronchogenic adenocarcinoma, metastatic pancreatic carcinoma, lymphoma and ovarian carcinoma\(^\text{22}\). A positive serum or pleural fluid mesothelin level is highly suggestive of pleural malignancy but a negative result cannot be considered reassuring.

**DIAGNOSTIC IMAGING:**

**Computed tomography (CT):**

CT scans may be performed in the investigation of undiagnosed exudative pleural effusions and can be useful in distinguishing malignant from benign pleural thickening. CT scans for pleural effusion should be performed with contrast before complete drainage of pleural fluid. CT scan should be requested for complicated pleural infection when initial tube drainage has been unsuccessful and surgery is to be considered.

On a CT, suspended air bubbles within the fluid imply septations though this finding is more reliable on ultrasound. CT is particularly helpful in the diagnosis of empyema when the pleural thickening is obvious around the fluid which usually forms a lenticular opacity. CT also distinguishes empyema from lung abscess. There are features of contrast-enhanced thoracic CT scanning which can help differentiate between benign and malignant disease. Malignant
effusion is suggested by the findings of, nodular pleural thickening, mediastinal pleural thickening, parietal pleural thickening >1 cm, and circumferential pleural thickening.

**Magnetic resonance imaging (MRI):**
MRI distinguishes accurately between benign and malignant pleural effusions. Distinction of morphological features of pleural malignancy by MRI has been shown in some studies to equal or even superior to CT or even superior while assessing diaphragmatic or chest wall involvement. MRI may be used to accurately assess pleural disease in patients for whom contrast is contraindicated.

**PET-CT imaging:**
The uptake of 18-fluorodeoxyglucose (FDG) has been shown to be greater in malignant pleural effusions. The value of PET-CT imaging in distinguishing benign from malignant disease is limited by false positives in patients with pleural inflammation (infection or following talc pleurodesis). PET-CT imaging does not currently have a role in the routine investigation of pleural effusions.

**INVASIVE TESTS:**
**Percutaneous pleural biopsy:**
In suspected malignancy, or if pleural nodularity is shown on contrast-enhanced CT, an image-guided cutting needle percutaneous pleural biopsy is the method of choice. Abrams needle biopsies are only diagnostically useful in areas with a high incidence of TB, although thoracoscopic and image-guided cutting needles have been shown to have a higher diagnostic yield. The diagnostic yield for Abrams pleural biopsy has been shown to be 57% for malignancy. The yield over pleural fluid cytology alone is increased by only 7-27% for malignancy. Complications of Abrams pleural biopsy include site pain (1-15%), pneumothorax (3-15%), vasovagal reaction (1-5%), haemothorax (<2%), site haematoma (<1%), transient fever (<1%) and, very rarely, death secondary to hemorrhage. This technique is particularly useful in patients who are unsuitable for thoracoscopy.

Image-guided cutting needle biopsies have shown to be superior to Abrams needle biopsies in the diagnostic yield for malignant disease. Abrams biopsy has shown to correctly diagnose malignancy in 8/17 patients (sensitivity 47%, specificity 100%) and CT-guided biopsy correctly diagnosed malignancy in 13/15 (sensitivity 87%, specificity 100%). While comparing thoracoscopy with Abrams biopsy in an area with a high prevalence of TB, thoracoscopy was found to have a combined culture/ histology sensitivity of 100% compared with 79% for Abrams pleural biopsy. Since blind pleural biopsy has reasonably high sensitivity and is likely to be more cost effective, it will often be the procedure of first choice in developing countries with a high incidence of TB. Blind pleural biopsy cannot be justified for the diagnosis of TB where the incidence is not high.

**Thoracoscopy:**
In patients with a symptomatic exudative pleural effusion where a diagnostic pleural aspiration is negative or inconclusive, and malignancy is suspected, thoracoscopy is suggested as the next choice investigation.

**Local anaesthetic thoracoscopy**
Local anaesthetic thoracoscopy can be performed by physicians or surgeons and is a safe and well tolerated procedure. Major complications (e.g., empyema, hemorrhage and pneumonia) occur in only 2.3% and death is rare. It has a diagnostic sensitivity for malignant pleural disease of 92.6%. It also has a higher diagnostic yield than blind pleural biopsy for tuberculous pleuritis. Talc poudrage can be administered at the end of the procedure which achieves a successful pleurodesis in 80-90%.

**Video-assisted thoracoscopic surgery (VATS)**
This is performed by thoracic surgeons and requires a general anaesthetic. Its contraindications are same as for general surgery. This procedure reports similarly high diagnostic sensitivity rates of approximately 95% for malignancy and is also relatively safe with a low complication rate. One advantage of VATS over local anaesthetic thoracoscopy is that during the procedure the surgeon can proceed to other thoracic surgical options if required.

**Bronchoscopy:**
Bronchoscopy is reserved for patients whose radiology suggests the presence of a mass or loss of volume or when there is a history of hemoptysis, possibility of aspiration of a foreign body or a trapped lung with a suspicion of a proximal lung mass. It should be performed after pleural drainage in order to eliminate the effect of extrinsic airway compression by pleural fluid.

**SPECIFIC CONDITIONS AND TESTS:**

**Tuberculous pleurisy:**
When pleural biopsies are taken, they should be sent for both histological examination and culture to improve the diagnostic sensitivity for TB. Thoracoscopic pleural biopsies are the test most likely to yield positive mycobacterial culture (and therefore drug sensitivity) results. Diagnostic markers of pleural TB are useful ‘rule out’ tests in low incidence countries. Adenosine deaminase is the most thoroughly validated to date.

Tuberculous effusion result from hypersensitivity reaction to mycobacterial protein and the mycobacterial load in the pleural fluid is usually low. Pleural fluid microscopy for acid-fast bacilli therefore has a sensitivity of <5% and pleural fluid culture of 10-20%. Thoracoscopic pleural biopsy has been shown to have a sensitivity of >70% for culture of pleural tissue and overall diagnostic sensitivity approaches 100% when evidence of caseating granulomas on pleural biopsy histology is combined with culture.

**Diagnostic markers of pleural TB:**
It is desirable to consider diagnosis of tuberculosis in patients with lymphocytic effusions. In patients who are unsuitable for invasive investigations, pleural fluid or blood biomarkers of infection can be useful.

*Adenosine deaminase (ADA)* is an enzyme present in lymphocytes, and its level in pleural fluid is significantly raised in most tuberculous pleural effusions. Raised ADA levels can also be seen in empyema, rheumatoid disease and occasionally in malignancy. Measurement of isoenzyme ADA-2 can reduce the false positives significantly. ADA is very cheap and quick to perform and remains stable when stored at 48°C for up to 28 days. It is useful in patients with HIV or those immunosuppressed (e.g., renal transplant). Being a highly sensitive test, ADA is a useful ‘rule out’ test in countries with low prevalence of TB.
**Interferon gamma release assays (IGRAs)** have been studied with sensitivities as high as 90%, but specificity is limited by an inability of the tests to distinguish latent from active TB. The commercial tests are not yet validated for fluids other than blood. Comparatively ADA is easier to perform and cost effective.

**Connective tissue diseases:**

Rheumatoid arthritis and systemic lupus erythematosus (SLE) are the most common connective tissue diseases to involve the pleura. Pleural effusions occur due to primary autoimmune pleuritis or secondary to renal, cardiac, thromboembolic disease or drug therapy.

**Rheumatoid arthritis-associated pleural effusions**

Pleural involvement occurs in 5% of patients with rheumatoid arthritis. Rheumatoid factor can be measured on the pleural fluid and often has a titer of $>1:320$. Most chronic pleural effusions secondary to rheumatoid arthritis have a very low glucose level of $<1.6$ mmol/l (29 mg/dl). Rheumatoid arthritis-associated pleural effusions occur more frequently in men, although the disease itself is more common in women. Chronic rheumatoid effusions are the most common cause of pseudochylous (high cholesterol) effusion but they can also be serous or hemorrhagic in appearance. The measurement of triglycerides and cholesterol in milky effusions will confirm the diagnosis of a pseudochylous picture. Eighty percent of rheumatoid pleural effusions have a pleural fluid glucose to serum ratio of $<0.5$ and a pH $<7.30$.

Measurement of C4 complement in pleural fluid may be of additional help, with levels $<0.04$ g/l in all cases of rheumatoid pleural disease.

**Systemic lupus erythematosus (SLE)**

Pleuritis is the first manifestation of SLE in 5-10% of patients and an early feature in 25-30%, and is usually accompanied by multisystem involvement. Pleural effusions are frequently small and are bilateral in 50% of patients.

No definitive test distinguishes SLE pleuritis from other causes of exudative effusions. Elevated pleural fluid antinuclear antibodies (ANA) and an increased pleural fluid to serum ANA ratio is suggestive of SLE pleuritis, but elevation is also sometimes seen in malignant effusions.

**Pulmonary embolism:**

Pleural effusions detectable on chest x-ray occur in 23-48% of patients with pulmonary embolism. Effusions are small in up to 90% of cases, although moderate and massive effusions are also recognized. They may be ipsilateral, contralateral or bilateral, relative to the radiologically-detected embolus. Recent series applying Light’s criteria have found that pleural effusions associated with pulmonary embolism are always exudates. Fluid characteristics, however, are non-specific and unhelpful in making the diagnosis which should be pursued radiologically, given a high index of clinical suspicion or in the context of an effusion that remains undiagnosed after standard baseline investigations.

**Chylothorax and pseudochylothorax:**

If a chylothorax (chylomicrons) or pseudochylothorax (cholesterol) is suspected, pleural fluid should be tested for cholesterol crystals and chylomicrons. Occasionally an empyema can be sufficiently turbid to be confused with chyle. They can be distinguished by bench centrifugation which leaves a clear supernatant in empyema while chylous effusion remains milky. It should be noted that, in starved patients, chyle may not appear milky.

Trauma, particularly following thoracic surgery, probably causes about 50% of the cases, while medical causes including malignancy (particularly lymphoma), TB and lymphatic malformations accounting for most of the remaining half. In non-surgical cases, a CT scan of the thorax to
exclude mediastinal pathology (especially lymphoma) is mandatory. The site of leak may be
demonstrated by lymphangiography.
Chylothorax must be distinguished from pseudochoylothorax or ‘cholesterol pleurisy’ which
results from the accumulation of cholesterol crystals. Rheumatoid pleurisy and tuberculous
pleuritis are the most commonly reported causes of a pseudochoylous effusion. Pseudochoylothorax usually arises from chronic (often years) pleural effusion and the pleura is
usually markedly thickened. A true chylothorax will usually have a high triglyceride level, usually >1.24 mmol/l (110 mg/dl) and can usually be excluded if the triglyceride level is <0.56 mmol/l (50 mg/dl). In a pseudochoylothorax a cholesterol level >5.18 mmol/l (200 mg/dl) or the presence of cholesterol crystals is diagnostic irrespective of triglyceride levels. Chylothorax can also result from transdiaphragmatic migration of chylous ascites due to hepatic cirrhosis but this is transudative.

**Pleural fluid lipid values in pseudochoylothorax and chylothorax:**

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<thead>
<tr>
<th>Feature</th>
<th>Pseudochoylothorax</th>
<th>Chylothorax</th>
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<tr>
<td>Triglycerides</td>
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<td>&gt;1.24 mmol/l (110 mg/dl)</td>
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<tr>
<td>Cholesterol</td>
<td>&gt;5.18 mmol/l (200 mg/dl)</td>
<td>Usually low</td>
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<tr>
<td>Cholesterol crystals</td>
<td>Often present</td>
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<tr>
<td>Chylomicrons</td>
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**Benign asbestos pleural effusion:**

Benign asbestos pleural effusions are commonly diagnosed in the first two decades after asbesots exposure. The prevalence is dose-related. The effusion is usually small and asymptomatic, often with pleural fluid which is hemorrhagic. There is a propensity for the effusion to resolve within 6 months, leaving behind residual diffuse pleural thickening. As there are no definitive tests, the diagnosis can only be made with certainty after a prolonged period of follow-up and consideration should be given to early thoracoscopy with pleural biopsy in any patient with a pleural effusion and a history of asbestos exposure, particularly in the presence of chest pain.

**MANAGEMENT OF PERSISTENT UNDIAGNOSED EFFUSIONS**

Even after a complete investigation including thoracoscopic biopsies, a significant number of patients with pleural exudates remain undiagnosed having label of ‘non-specific pleuritis’. About 8% of such effusions subsequently turn out to be malignant during follow up period. The majority of patients with non-specific pleuritis follow a benign course, with spontaneous resolution in 82% of the cases. In patients not fit enough for thoracoscopy, it is sensible to reconsider diagnoses with a specific treatment (eg, TB, pulmonary embolism, lymphoma and chronic heart failure). A considerable number of undiagnosed pleural effusions in this category are due to a malignant process. Close observation during follow up is the appropriate management.

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