Pleural disease

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Abstract

Pleural disease encompasses a wide range of pathological processes, many of which are common and increasing in incidence. Patients with pleural disease are encountered by both respiratory specialists and general physicians, and a systematic approach to their management helps in targeting investigation and optimizing patient care. Research has led to recent advances in diagnostic strategies and therapeutic techniques in these patients. This review focuses on the clinical assessment, diagnosis and management of patients with pleural effusions, malignant pleural disease, pleural infection and pneumothorax, and provides practical suggestions regarding investigation and management.

Keywords Empyema; malignant pleural effusion; parapneumonic effusion; pleural disease; pleural effusion; pneumothorax

Key points

- Point-of-care ultrasound guidance should be used for all pleural procedures involving fluid
- If the pleural fluid protein concentration is 25–35 g/litre, Light's criteria can be used to differentiate exudates from transudates
- Pleural fluid pH should be measured in all non-purulent effusions if infection is suspected; pH <7.2 indicates a need for tube drainage
- Only 60% of malignant effusions can be diagnosed by cytology
- Image-guided pleural biopsy has a higher diagnostic yield than blind pleural biopsy for malignancy
- Indwelling pleural catheters are increasingly being used to manage symptomatic malignant pleural effusions, reducing hospitalization and enabling management in the community
- Pleural fluid specimens for microbiology should be sent in both a sterile tube (for Gram stain, acid- and alkali-fast bacilli and culture of *Mycobacterium tuberculosis*) and blood culture bottles to increase the microbiological yield
- Combination treatment with intrapleural tissue-type plasminogen activator and DNase may be beneficial in patients with pleural infection resistant to standard medical therapy
- Heimlich valves allow ambulatory treatment for selected patients with pneumothorax

Investigating pleural effusions

Pleural effusions are a common medical problem (Table 1). There are several underlying mechanisms, including:

- increased permeability of the pleural membrane
- increased pulmonary capillary pressure
- excess negative intrapleural pressure
- reduced tissue oncotic pressure
- obstructed lymphatic flow.

The differential diagnosis is wide, so a systematic approach to investigation is necessary.[1] This should start with an accurate history, including a drug history (Table 2), and examination.

Pleural aspiration: a diagnostic pleural fluid sample should be collected using a fine-bore (21 G) needle and a 50-ml syringe, using ultrasound guidance to locate a safe site to perform the procedure (Table 3).[1]

The appearance and odour of the fluid should be noted. The sample should be placed in sterile vials, blood culture bottles and a heparinized syringe (to measure pH using a blood gas analyser) and sent for the following tests:

- biochemistry – lactate dehydrogenase (LDH), total protein, glucose
- microbiology – Gram stain, identification of acid- and alcohol-fast bacilli (AAFB) and microbiological culture
- cytology
- pH.

Distinguishing pleural fluid exudate and transudate: in most cases, a pleural fluid total protein of less than 25 g/litre represents a transudate and more than 35 g/litre an exudate. However, if the serum total protein is low or the pleural fluid protein concentration lies between these figures, differentiating the two can be more difficult. In these cases, measurement of serum and pleural fluid LDH and total protein allows Light's criteria to be used to distinguish exudates and transudates more accurately (Table 4).

Light's criteria have good sensitivity and specificity (as high as 98% in some series). However, a small number of patients with malignancy will be categorized as having a transudate; in addition, patients with cardiac failure taking diuretics may have a higher fluid protein concentration, so the pleural fluid may be mislabelled as an exudate.

Differential cell counts: a differential count of a pleural fluid sample can be useful in narrowing the differential diagnosis, but the results are not disease-specific. Lymphocytic effusions are commonly seen in malignancy and tuberculosis (TB), after coronary artery bypass graft and with cardiac failure and chronic pleural effusions.

Neutrophilic effusions usually signify a more acute disease process, such as pulmonary emboli (PEs) or parapneumonic effusions.

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Causes of transudative and exudative pleural effusions

Transudative	Exudative
Common	*Common*
Left ventricular failure	Malignancy
Cirrhosis	Parapneumonic effusions
Hypoalbuminaemia	*Less common*
Peritoneal dialysis	Pulmonary infarction
Less common	Rheumatoid arthritis
Hypothyroidism	Autoimmune diseases
Renal impairment	Benign asbestos effusion
Mitral stenosis	Post-myocardial infarction syndrome
Pulmonary embolism	*Rare*
Rare	Yellow nail syndrome
Constrictive pericarditis	Drugs (Table 2)
Superior vena cava obstruction	
Ovarian hyperstimulation	

Table 1

pH: a low pleural fluid pH (<7.2) can indicate pleural infection requiring chest tube drainage. Other causes of low pH effusions include advanced malignancy, rheumatoid arthritis, TB, collagen vascular disease and oesophageal perforation. Pleural fluid glucose concentration correlates with pleural fluid pH and can be a useful alternative if pH cannot be measured.

Cytology: malignant effusions can be diagnosed from a single pleural fluid cytology specimen in about 60% of cases. A second cytology specimen increases the yield slightly. Certain malignant cell types are diagnosed more readily by experienced cytologists, using immunocytochemistry; a cytological diagnosis is more likely in a malignant pleural effusion due to metastatic adenocarcinoma than in mesothelioma for instance.

Pleural imaging: effusions greater than 200 ml can be detected on a postero-anterior chest radiograph, although smaller volumes can be detected using thoracic ultrasound. Ultrasound scanning can also differentiate more clearly between pleural fluid and thickening, assess septations and loculations within an effusion and help to identify a safe site for pleural procedures.

Computed tomography (CT) can help to characterize pleural abnormalities further. Contrast enhancement aids differentiation between benign and malignant pleural thickening and is often visualized more clearly if some pleural fluid is still present (Figure 1). In addition, CT can identify other underlying causes of a pleural effusion, such as PEs, infection or tumours. Up to 40% of patients with PEs have a small pleural effusion with no specific biochemical characteristics; a high index of suspicion is required to make this diagnosis, and CT pulmonary angiography should be requested if the diagnosis is considered.

Magnetic resonance imaging (MRI) is developing as an imaging modality for pleural disease and can be useful in selected cases where clear soft tissue differentiation is required.

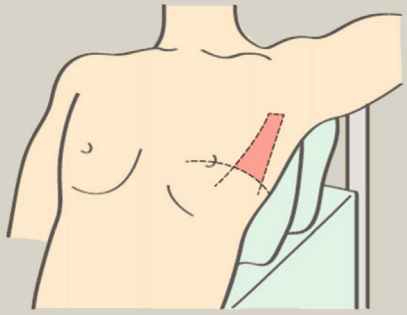
Drug causes of pleural effusion

Common	Rare
Amiodarone	Carbamazepine
Nitrofurantoin	Penicillamine
Phenytoin	Cyclophosphamide
Methotrexate	Bromocriptine
Cabergoline	
Pergolide	
Dasatinib	

Table 2

Pleural procedures[1]

- Pleural procedures should not take place out of hours except in an emergency
- Pleural aspirations and chest drain should be inserted in a clean environment using full aseptic technique
- Bedside thoracic ultrasound guidance is strongly recommended for all pleural procedures involving pleural fluid
- The preferred site for pleural interventions is the triangle of safety (see below)
- Non-urgent pleural procedures should be avoided in anti-coagulated patients until the international normalized ratio is <1.5
- Pleural fluid aspiration should be stopped when no more fluid can be aspirated or the patient becomes symptomatic, to reduce the risk of re-expansion pulmonary oedema. The total amount aspirated is often limited to 1.5 litres in the elderly.



Identify the 'safe triangle for drain placement, as demarcated by the outer border of the pectoralis major, the anterior border of the latissimus dorsi and a horizontal line that meets the nipple anteriorly. In general, the drain should be sited in the 4th or 5th intercostal space within this triangle.

Table 3

Light's criteria

Pleural fluid is an exudate if one or more of the following criteria are met:

- Pleural fluid protein:serum protein ratio >0.5
- Pleural fluid LDH:serum LDH ratio >0.6
- Pleural fluid LDH more than two-thirds of upper limit of normal serum LDH

LDH, lactate dehydrogenase.

Table 4