INTRODUCTION

The following is a summary of the British Thoracic Society (BTS) Guideline for pleural disease and includes a summary of the guideline recommendations and good practice points (GPPs). The full guideline is published as a separate Thorax Supplement and is available from the BTS website. Please refer to the full guideline for full information about each section. All online supplemental appendices are also available via the BTS website.

BACKGROUND

The aim of the guideline was to provide evidence-based guidance on the investigation and management of pleural disease. Pleural disease is common and represents a major and rapidly developing subspecialty that presents to many different hospital services. Since the last BTS Guideline for pleural disease published in 2010, many high quality and practice changing studies, using patient centred outcomes, have been published. The paradigms for the investigation and management of pleural disease have therefore shifted, so this guideline aimed to capture this evidence and use it to answer the most important questions relevant to today’s practice.

Target audience for the guideline

The guideline will be of interest to UK based clinicians caring for adults with pleural disease, including chest physicians, respiratory trainees, specialist respiratory nurses, specialist lung cancer nurses, specialist pleural disease nurses, pathologists, thoracic surgeons, thoracic surgeon trainees, acute physicians, oncologists, emergency physicians, hospital practitioners, intensive care physicians, palliative care physicians, radiologists, other allied health professional and patients and carers.

Areas covered by the guideline

The guideline focuses on the investigation and management of pleural disease in adults and covers four broad areas of pleural disease:

a. Spontaneous pneumothorax
b. Undiagnosed unilateral pleural effusion
c. Pleural infection
d. Pleural malignancy

Adult patients in both inpatient and ambulatory settings are considered.

The guideline does not cover mesothelioma (as alternative guidance is available), benign (non-infectious, non-pneumothorax) pleural disease or rare pleural diseases. Guidance on pleural interventions is also covered in the BTS Clinical Statement on Pleural Procedures.

Methodology

BTS guidelines use the GRADE (Grading of Recommendations, Assessment, Development and Evaluations) methodology for guideline development. GRADE is a systematic and transparent process for assessing the quality of the evidence and the full GRADE process involves:

i. Systematic review
ii. Critical appraisal; and
iii. GRADE analysis.

Full details of the BTS process are available in the BTS Guideline production manual (https://www.brit-thoracic.org.uk/quality-improvement/guidelines/).

Clinical questions, patient-centred outcomes and literature search

Clinical questions were defined from the scope of the guideline formulated into PICO (population, intervention, comparator, and outcome) style framework diagnostic accuracy, intervention or prognostic review formats. Patient-centred outcomes were agreed by the group for each question. The PICO framework formed the basis of the literature search. The initial searches were completed by the University of York, and the latter stages by BTS Head Office. Systematic electronic database searches were conducted to identify all papers that may be relevant to the guideline. For each question, the following databases were searched: Cochrane Database of Systematic Reviews (CDSR), Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE. The search strategy is available for review in Online Appendix 1 (accessible via the full guideline).

Critical appraisal and GRADE analysis of the evidence

After an initial screening to determine relevance to the clinical questions, each paper was assessed to determine if it addressed:
In some instances where evidence was limited, but GDG members felt it was important to include a recommendation rather than a GPP, recommendations were agreed by informal consensus and categorised as (Conditional – by consensus), based on the same criteria detailed in table 1.

### Stakeholders
Stakeholders were identified at the start of the process. All stakeholder organisations were notified when the guideline was available for public consultation and a list of all stakeholders is listed in Appendix 4 to the full guideline.

### SUMMARY OF RECOMMENDATIONS AND GOOD PRACTICE POINTS

#### Spontaneous pneumothorax

**Acute management for spontaneous pneumothorax**

**Recommendations**
- Conservative management can be considered for the treatment of minimally symptomatic (ie, no significant pain or breathlessness and no physiological compromise) or asymptomatic primary spontaneous pneumothorax in adults regardless of size. (Conditional – by consensus)
- Ambulatory management should be considered for the initial treatment of primary spontaneous pneumothorax in adults with good support and in centres with available expertise and follow-up facilities. (Conditional)
- In patients not deemed suitable for conservative or ambulatory management, needle aspiration or tube drainage should be considered for the initial treatment of primary spontaneous pneumothorax in adults. (Conditional)
- Chemical pleurodesis can be considered for the prevention of recurrence of secondary spontaneous pneumothorax in adults (eg, patients with severe COPD who significantly decompensated in the presence of a pneumothorax, even during / or after the first episode). (Conditional)
- Thoracic surgery can be considered for the treatment of pneumothorax in adults at initial presentation if recurrence prevention is deemed important (eg, patients presenting with tension pneumothorax, or those in high risk occupations). (Conditional)

**Good practice points**
- When establishing local ambulatory treatment pathways, planning and coordination between with the emergency department, general medicine and respiratory medicine is vital.
- When performing chemical pleurodesis for the treatment of pneumothorax in adults, adequate analgesia should be provided before and after treatment.
- All treatment options should be discussed with the patient to determine their main priority, with consideration for the least invasive option.
Optimal management after the resolution of a first episode of pneumothorax

**Good practice points**

- Elective surgery may be considered for patients in whom recurrence prevention is deemed important (e.g., at risk professionals (divers, airline pilots, military personnel), or those who developed a tension pneumothorax at first episode).
- Elective surgery should be considered for patients with a second ipsilateral or first contralateral pneumothorax.
- Discharge and activity advice should be given to all patients post pneumothorax.

Optimal management for spontaneous pneumothorax and ongoing air leak

**Good practice point**

- If a patient is not considered fit for surgery, autologous blood pleurodesis or endobronchial therapies should be considered for the treatment of pneumothorax with persistent air leak in adults.

Optimal surgical approach and surgical operation for pneumothorax management

**Recommendations**

- Video-assisted thoracoscopy access can be considered for surgical pleurodesis in the general management of pneumothorax in adults. (Conditional)
- Thoracotomy access and surgical pleurodesis should be considered for the lowest level of recurrence risk required for specific (e.g., high risk) occupations. (Conditional)
- Surgical pleurodesis and/or bullectomy should be considered for the treatment of spontaneous pneumothorax in adults. (Conditional)

Investigation of the undiagnosed unilateral pleural effusion

**Radiology for diagnosing unilateral pleural effusions of benign aetiology**

**Good practice points**

- Imaging findings of a unilateral pleural effusion should be interpreted in the context of clinical history and knowledge of pleural fluid characteristics.
- CT follow-up should be considered for patients presenting with pleural infection to exclude occult malignancy if there are ongoing symptoms, or other clinically concerning features.
- PET-CT should not be used in the assessment of pleural infection.

**Image guided versus non-image guided intervention for suspected unilateral pleural effusion**

**Recommendation**

- Image-guided thoracentesis should always be used to reduce the risk of complications. (Strong – by consensus)

Optimal volume and container for pleural aspiration samples

**Recommendations**

- 25–50 mL of pleural fluid should be submitted for cytological analysis in patients with suspected malignant pleural effusion (MPE). (Strong – by consensus)
- Pleural fluid should be sent in both plain and blood culture bottle tubes in patients with suspected pleural infection. (Strong – by consensus)

**Guideline summary**

**Pleural fluid tests (biomarkers) for diagnosing unilateral pleural effusion**

**Recommendations**

- Pleural fluid cytology should be used as an initial diagnostic test in patients with suspected secondary pleural malignancy, accepting that a negative cytology should lead to consideration of further investigation. (Conditional)
- Pleural fluid biomarkers should not be used for diagnosing secondary pleural malignancy. (Conditional)
- In high prevalence populations, pleural fluid adenosine deaminase (ADA) and/or interferon gamma (IFN-gamma) test(s) can be considered for diagnosing tuberculous pleural effusion. (Conditional)
- In low prevalence populations, pleural fluid adenosine deaminase (ADA) can be considered as an exclusion test for tuberculous pleural effusion. (Conditional)
- Tissue sampling for culture and sensitivity should be the preferred option for all patients with suspected tuberculous pleural effusion. (Strong – by consensus)
- Pleural fluid antinuclear antibody (ANA) should be considered to support a diagnosis of lupus pleuritis. (Conditional)

**Good practice points**

- The clinical utility of pleural fluid cytology varies by tumour sub-type, including diagnostic sensitivity and predictive value for response to subsequent cancer therapies. This should be taken into consideration when planning the most suitable diagnostic strategy (for example, direct biopsies in those with a likely low cytological yield can be considered).
- Pleural fluid N-terminal pro brain natriuretic peptide (NT-proBNP) is useful when considering heart failure as a cause in unilateral pleural effusions but not superior to serum NT-proBNP and therefore should not be ordered routinely.

**Serum biomarkers for diagnosing unilateral pleural effusion**

**Recommendations**

- Serum NT-proBNP should be considered to support a diagnosis of heart failure in patients with unilateral pleural effusion suspected of having heart failure. (Conditional)
Guideline summary

Good practice points
✓ Serum biomarkers should not currently be used to diagnose secondary pleural malignancy, pleural infection or autoimmune pleuritis.
✓ Serum biomarkers should not routinely be used to diagnosis tuberculous pleural effusion, but may be considered in high prevalence areas.
✓ Serum biomarkers, including NT-proBNP, should not be used in isolation for diagnosing unilateral pleural effusion, as multiple conditions may co-exist.

Pleural biopsy for diagnosing unilateral pleural effusion
Recommendations
► Thoracoscopic or image-guided pleural biopsy may be used depending on the clinical indication and local availability of techniques (including need for control of pleural fluid). (Strong)
► Blind (non-image guided) pleural biopsies should not be conducted. (Strong – by consensus)

Pleural infection
Predicting clinical outcomes of pleural infection
Recommendation
► RAPID (renal, age, purulence, infection source, dietary factors) scoring should be considered for risk stratifying adults with pleural infection and can be used to inform discussions with patients regarding potential outcome from infection. (Conditional)

Pleural fluid, or radiology parameters for determining which patients can be treated with intercostal drainage
Recommendations
► For patients with parapneumonic effusion (PPE) or suspected pleural infection, where diagnostic aspiration does not yield frank pus, immediate pH analysis should be performed. (Strong – by consensus)
► For patients with suspected complex parapneumonic effusion (CPPE):
  - If pleural fluid pH \( \leq 7.2 \) this implies a high risk of CPPE or pleural infection and an intercostal drain (ICD) should be inserted if the volume of accessible pleural fluid on ultrasound makes it safe to do so. (Strong – by consensus)
  - If pleural fluid pH is \( > 7.2 \) and \( < 7.4 \) this implies an intermediate risk of CPPE or pleural infection. Pleural fluid lactate dehydrogenase (LDH) should be measured and if \( > 900 \) IU/L intercostal drainage should be considered, especially if other clinical parameters support CPPE (specifically ongoing temperature, high pleural fluid volume, low pleural fluid glucose (72 mg/dL \( \leq 4.0 \) mmol/L), pleural contrast enhancement on CT or septation on ultrasound. (Strong – by consensus)
  - If pleural fluid pH \( \geq 7.4 \) this implies a low risk of CPPE or pleural infection and there is no indication for immediate drain. (Strong – by consensus)
► In the absence of readily available immediate pleural fluid pH measurement, an initial pleural fluid glucose <3.3 mmol/L may be used as an indicator of high probability of CPPE/pleural infection and can be used to inform decision to insert intercostal drain in the appropriate clinical context. (Strong – by consensus)

Good practice points
✓ Clinicians should be mindful of alternative diagnoses that can mimic parapneumonic effusion (PPE) with a low pH and potential for loculations (eg, rheumatoid effusion, effusions due to advanced malignancy/mesothelioma).
✓ Pleural fluid samples taken for pH measurement should not be contaminated with local anaesthetic or heparin (eg, by extruding all heparin from an arterial blood gas syringe) as this lowers pleural fluid pH. Delays in obtaining a pleural fluid pH will also increase pleural fluid pH.
✓ In patients where a clinical decision is made not to insert an ICD at initial diagnostic aspiration, regular clinical reviews should be performed and repeat thoracocentesis considered to ensure that CPPE is not missed.

Optimal initial drainage strategy for established pleural infection
Recommendation
► Initial drainage of pleural infection should be undertaken using a small bore chest tube (14F or smaller). (Conditional – by consensus)

Intrapleural therapy for managing pleural infection
Recommendations
► Combination tissue plasminogen activator (TPA) and DNase should be considered for the treatment of pleural infection, where initial chest tube drainage has ceased and leaves a residual pleural collection. (Conditional – by consensus)
► Saline irrigation can be considered for the treatment of pleural infection when intrapleural TPA and DNase therapy or surgery is not suitable. (Conditional – by consensus)
► Single agent tissue plasminogen activator (TPA) or DNase should not be considered for treatment of pleural infection. (Conditional – by consensus)
► Streptokinase should not be considered for treatment of pleural infection. (Conditional)

Good practice points
✓ Patient consent should be taken when using TPA and DNase as there is a potential risk of bleeding.
✓ When administering TPA plus DNase the regime should be 10 mg TPA twice daily (10 mg two times per day)+5 mg DNase two times per day for 3 days, based on randomised controlled trial data. Based on retrospective case series data, lower dose 5 mg TPA two times per day+5 mg DNase two times per day for 3 days may be as effective, and can be used if considered necessary.
✓ Reduced doses of TPA may be considered in those with a potentially higher bleeding risk (eg, those on therapeutic anticoagulation which cannot be temporarily ceased).
✓ For details on administration of intrapleural treatments, please refer to the BTS Clinical Statement on Pleural Procedures.11

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ATS
Optimal surgical approach and surgical method for managing pleural infection

**Recommendation**
- VATS access should be considered over thoracotomy for adults in the surgical management of pleural infection. (Conditional)

**Good practice points**
- When selecting a surgical access for the treatment of pleural infection in adults, it is important to ensure the technique can facilitate optimal clearance of infected material and achieve lung re-expansion where appropriate.
- Extent of surgery should be tailored according to patient and empyema stage when the lung is not completely trapped (drainage vs debridement).
- Decortication should be a decision that is individualised to the patient with a trapped lung based on assessment of patient fitness and empyema stage.

**Pleural malignancy**

Optimal imaging modality for diagnosing pleural malignancy

**Recommendations**
- Ultrasound may be a useful tool at presentation to support a diagnosis of pleural malignancy, particularly in the context of a pleural effusion, where appropriate sonographic skills are present. (Conditional)
- CT allows assessment of the entire thorax, and positive findings may support a clinical diagnosis of pleural malignancy when biopsy is not an option (Conditional), however a negative CT does not exclude malignancy. (Strong – by consensus)
- PET-CT can be considered to support a diagnosis of pleural malignancy in adults when there are suspicious CT or clinical features and negative histological results, or when invasive sampling is not an option. (Conditional)

**Good practice points**
- Imaging can play an important role in the assessment of pleural malignancy, but results should be interpreted in the context of clinical, histological and biochemical markers.
- Features of malignancy may not be present on imaging at presentation. Unless a clear diagnosis is reached by other means (eg, biopsy), monitoring with follow-up imaging of patients presenting with pleural thickening and unexplained unilateral pleural effusion should be considered to exclude occult malignancy.
- MRI has potential as a diagnostic tool in pleural malignancy. Its clinical value has yet to be determined and its use should be limited to highly selected cases and research studies at the present time.

Systemic therapy for reducing the need for definitive pleural intervention for malignant pleural effusion

**Recommendation**
- Definitive pleural intervention should not be deferred until after systemic anti-cancer therapy (SACT). (Conditional – by consensus)

Managing malignant pleural effusion

Pleural aspiration with no pleurodesis agent versus talc slurry pleurodesis

**Recommendation**
- Management of malignant pleural effusion (MPE) using talc pleurodesis (or another method) is recommended in preference to repeated aspiration especially in those with a better prognosis, but the relative risks and benefits should be discussed with the patient. (Conditional – by consensus)

**Indwelling pleural catheter versus talc slurry pleurodesis**

**Recommendation**
- Patients without known non-expandable lung should be offered a choice of indwelling pleural catheter (IPC) or pleurodesis as first line intervention in the management of MPE. The relative risks and benefits should be discussed with patients to individualise treatment choice. (Conditional)

**Good practice points**
- The psychological implications and potential altered body image aspects of having a semi-permanent tube drain in situ should not be underestimated and must be considered prior to insertion.
- All patients who have had an IPC inserted should be referred to the community nursing team on discharge for an early assessment of the wound site, symptom control, support with IPC drainage and removal of sutures.
- Patients and their relatives should be supported to perform community drainage and complete a drainage diary if they feel able to do so, to promote independence and self-management.
- Complications such as infection refractory to community management, suspected drain fracture, loculations or blockage with persistent breathlessness should be referred back to the primary pleural team for further assessment.

Thoracoscopy and talc poudrage pleurodesis versus chest drain and talc slurry pleurodesis

**Recommendation**
- Talc slurry or talc poudrage may be offered to patients with MPE to control fluid and reduce the need for repeated procedures. (Conditional)

**Good practice point**
- Where a diagnostic procedure is being conducted at thoracoscopy (pleural biopsies), if talc pleurodesis is reasonable, this should be conducted during the same procedure via poudrage.

Surgical pleurodesis, or surgical decortication versus talc slurry pleurodesis

**Recommendation**
- In selected patients considered fit enough for surgery, either surgical talc pleurodesis or medical talc slurry can be considered for the management of patients with MPE. The relative risks, benefits and availability of both techniques should be discussed with patients to individualise treatment choice. (Conditional – by consensus)
Guideline summary

Good practice points

- Informed decision-making should include the role of surgery versus ambulatory management with an IPC for the management of MPE in selected patients.
- Decortication surgery may improve pleurodesis success in malignant pleural effusion patients with non-expandable lung, but the risks and benefits of IPC and surgical treatment should be discussed with patients, and treatment individualised according to circumstances (for example, fitness to undergo thoracic surgery).

Managing malignant pleural effusion and non-expandable lung

Pleural aspiration, talc slurry pleurodesis, talc poudrage pleurodesis, decortication surgery or indwelling pleural catheter (IPC)

Good practice points

- Decisions on treatment modality for malignant pleural effusion and non-expanded lung should be based on patient choice, with the relative risks and benefits of each modality discussed with the patient, but patients should be made aware of the limited evidence base regarding treatment options for non-expandable lung.
- IPCs are effective at controlling symptoms in non-expandable lung and should be considered, but it may be appropriate to undertake pleural aspiration first to assess symptomatic response.
- Pleural aspiration may result in a need for multiple procedures so alternatives should be discussed with the patient.
- In patients with radiologically significant (>25%) non-expandable lung requiring intervention for a symptomatic MPE, current evidence suggests the use of an indwelling pleural catheter rather than talc pleurodesis.
- In MPE patients with less than 25% non-expandable lung, talc slurry pleurodesis may improve quality of life, chest pain, breathlessness and pleurodesis rates.
- Decortication surgery may improve pleurodesis success in selected MPE patients with non-expanded lung, but the risks and benefits of IPC and surgical treatment should be discussed with patients, and treatment individualised according to circumstances (for example, fitness to undergo thoracic surgery).

Managing malignant pleural effusion and septated effusion

(on radiology)

Intrapleural enzymes versus surgery, or no treatment

Good practice points

- Intrapleural fibrinolytics can be considered in highly selected symptomatic patients with MPE to try to improve breathlessness.
- Intrapleural fibrinolytics may be used in patients with MPE and septated effusion and an indwelling pleural catheter (IPC) to improve drainage if flushing the IPC with normal saline or heparinised saline does not improve drainage.
- Surgery can be considered for palliation of symptoms in a minority of patients with significantly septated MPE and associated symptoms and otherwise good prognosis and performance status.

Managing malignant pleural effusion treated with an indwelling pleural catheter (IPC)

Symptom-based/conservative drainage versus daily drainage

Recommendations

- Where IPC removal is a priority, daily IPC drainages are recommended to offer increased rates of pleurodesis when compared with less frequent drainages of symptom-guided or alternate drainage regimes. (Conditional)
- Patients should be advised that they do not require daily drainage to control symptoms of breathlessness and chest pain if they wish to opt for a less intensive regime. (Strong – by consensus)

Good practice points

- Decisions on the optimal drainage should be based on patient choice.
- Informed decision making should include the explanation of the effect of drainage regimes on the patient-centre outcomes such as breathlessness and the possibility of auto-pleurodesis during the disease course.
- Although daily drainage may result in earlier removal of IPC, there may be an associated cost associated with the increased number of drainage events (both to the healthcare system, and to the patient). This has been addressed in a modelling study and should be considered.

Intrapleural agents (talc or other pleurodesis agents)

Recommendation

- Instillation of talc via an indwelling pleural catheter (IPC) should be offered to patients with expandable lung where the clinician or patient deems achieving pleurodesis and IPC removal to be important. (Conditional – by consensus)

Intrapleural chemotherapy versus systemic treatment for treating pleural malignancy

Recommendation

- Intrapleural chemotherapy should not be routinely used for the treatment of MPE. (Conditional – by consensus)

Good practice point

- All patients of good performance status with metastatic malignancy should be considered for systemic anti-cancer therapy (SACT) as standard of care as per national guidelines.

Using prognostic or predictive scores to provide prognostic information for patients with malignant pleural effusion

Good practice points

- Clinicians may consider using a validated risk score for malignant pleural effusion if the information is of use in planning treatments or in discussion with patients.
- Patients with pleural malignancy should be managed in a multi-disciplinary way, including referral to specialist palliative care services where appropriate.

Healthcare providers need to use clinical judgement, knowledge and expertise when deciding whether it is appropriate to apply recommendations for the management of patients. The recommendations cited here are a guide and may not be appropriate for use in all situations. The guidance provided does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.

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REFERENCES
APPENDIX 1 – CLINICAL PATHWAYS/DECISION TREES

Pneumothorax Pathway

High risk characteristics:
1. Haemodynamic compromise (tension pneumothorax)
2. Significant hypoxia
3. Bilateral pneumothorax
4. Underlying lung disease
5. ≥ 50 years of age with significant smoking history
6. Haemopneumothorax

Is the patient symptomatic?

Safe to intervene? (Pneumothorax sufficient)

What is the patient’s main priority?

Procedure avoidance

Rapid symptom relief (ambulatory)¹

Rapid symptom relief (short-term drainage)

CT imaging and reassess

Take into account
- Patient preference
- Local availability

Conservative care

PSP
Regular review as outpatient (every 2-4 days)²

SSP
Review inpatient

If stable, follow-up in OPD in 2-4 weeks

Ambulatory device

Regular review as outpatient (every 2-3 days)²

Remove device when resolved

If stable, follow-up in OPD in 2-4 weeks

Needle aspiration

Resolved?³

YES

Discharge & review in OPD in 2-4 weeks

NO

Chest drain

Regular review as inpatient (daily)

Remove drain when resolved⁴

Discharge & review in OPD in 2-4 weeks

* Pneumothorax of sufficient size to intervene depends on clinical context but, in general, usually ≥ 2cm laterally or apically on CXR, or any size on CT scan which can be safely accessed with radiological support.

¹ If ambulatory pathway available locally.

² At review, if enlarging pneumothorax or symptoms consider chest drain insertion and admission.

³ Success: improvement in symptoms and sustained improvement on CXR.

⁴ Talc pleurodesis can be considered on the first episode of pneumothorax in high risk patients in whom repeat pneumothorax would be hazardous (eg, severe COPD).

CXR, chest X-ray; COPD, chronic obstructive pulmonary disease; OPD, outpatient department; PSP, primary spontaneous pneumothorax; SSP, secondary spontaneous pneumothorax.
Unilateral pleural effusion diagnostic pathway

**Guideline summary**

CXR, chest X-ray; FBC, full blood count; LDH, lactate dehydrogenase; NT-proBNP, N-terminal prohormone brain natriuretic peptide; PE, pulmonary embolism; TB, tuberculosis; TUS, thoracic ultrasound.

1. **History, clinical examination, CXR and assessment with thoracic ultrasound**
   - Is pleural malignancy suspected?
     - **YES**
       - Staging CT scan
     - **NO**
       - Is it safe to perform pleural aspiration?
         - YES
           - A contrast enhanced CT thorax, abdomen and pelvis should be performed
           - Undertake a pleural aspiration using ultrasound guidance
           - Send for: cytology, protein, LDH, glucose, pH and MC&S as appropriate
           - If ultrasound reveals a good target for obtaining pleural tissue – consider performing TUS guiding cutting needle biopsy at the same time
           - If patient has history of previous asbestos exposure and mesothelioma suspected, consider going straight to thoracoscopy
         - **NO**
           - Is it safe to perform pleural aspiration?
             - YES
               - Perform a pleural aspiration, using ultrasound guidance.
               - Send for: cytology, protein, LDH, glucose, pH and MC&S as appropriate
               - (Additional pleural tests if warranted – See Box 1)
               - Blood tests should include C-reactive protein, FBC, renal, liver function tests and albumin
               - (Additional blood and/or blood tests if warranted – See Box 1)
               - (See Tables 1-6 on the next two pages for interpretation of results and causes)
               - Unless pleural infection is the cause a contrast enhanced CT thorax should be performed. It will add value in most cases and help exclude dual pathology
             - **NO**
               - CT scan and treat the cause
           - **NO**
             - Cause found?
               - YES
                 - Treat appropriately
               - NO
                 - If not already performed consider a radiology guided pleural biopsy or thoracoscopy
                 - PET imaging in selected cases might help with management
                 - Re-consider treatable conditions such as PE, TB, chronic heart failure and lymphoma.
                 - If felt to be a benign cause but malignancy not fully excluded – interval CT imaging advised

**Box 1: Additional pleural fluid tests and blood tests**

<table>
<thead>
<tr>
<th>SUSPECTED DISEASE</th>
<th>TESTS</th>
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<tbody>
<tr>
<td>Chylothorax</td>
<td>- pf cholesterol and triglyceride</td>
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<tr>
<td>Haemothorax</td>
<td>- pf haematocrit</td>
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<tr>
<td>Empyema</td>
<td>- pf centrifuge</td>
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<tr>
<td>Rheumatoid disease</td>
<td>- pf glucose and pH</td>
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<tr>
<td>Pancreatitis</td>
<td>- serum lipase</td>
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<tr>
<td>Cardiac failure</td>
<td>- serum NT-ProBNP</td>
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<tr>
<td>Lymphoma</td>
<td>- pf lymphocyte subsets</td>
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<td>Autoimmune disease</td>
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<tr>
<td>IgG4 disease</td>
<td>- pleural biopsy and serum IgG4</td>
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<tr>
<td>Amyloid</td>
<td>- Congo red staining</td>
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CXR, chest X-ray; FBC, full blood count; LDH, lactate dehydrogenase; NT-proBNP, N-terminal prohormone brain natriuretic peptide; PE, pulmonary embolism; TB, tuberculosis; TUS, thoracic ultrasound.
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Unilateral pleural effusion diagnostic pathway – Tables 1-6

Table 1

Light’s criteria

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

- Pleural fluid protein divided by serum protein is >0.5
- Pleural fluid lactate dehydrogenase (LDH) divided by serum LDH is >0.6
- Pleural fluid LDH >2/3 the upper limits of laboratory normal value for serum LDH

Table 2

Transudates | Exudates
---|---
Common
- Congestive cardiac failure
- Liver cirrhosis
- Hypoalbuminaemia
- Nephrotic syndrome

Less common
- Nephrotic syndrome
- Mitral stenosis
- Peritoneal dialysis
- Chronic hypothyroidism
- Constrictive pericarditis

Common
- Malignancy
- Pleural infection
- Pulmonary embolism
- Autoimmune pleuritis

Less common
- Drugs
- Lymphatic disorders
- Meigs syndrome
- Post-coronary artery bypass graft
- Benign asbestos related pleural effusion

Table 3

Causes of lymphocytic pleural effusion

Malignancy
Tuberculosis
Lymphoma
Congestive cardiac failure
Post-coronary bypass graft
Rheumatoid arthritis
Chylothorax
Yellow nail syndrome

Table 4

Causes of bilateral pleural effusions

Congestive cardiac failure
Hypoalbuminaemia
Renal failure
Liver failure
SLE and other autoimmune diseases
Widespread malignancy including abdominal/pelvic malignancy
Bilateral pulmonary embolus
Table 5

<table>
<thead>
<tr>
<th>Pleural fluid lipid values in chylothorax and pseudochylothorax</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chylothorax:</strong></td>
</tr>
<tr>
<td>• Triglycerides</td>
</tr>
<tr>
<td>• Cholesterol</td>
</tr>
<tr>
<td>• Cholesterol crystals</td>
</tr>
<tr>
<td>• Chylomicrons</td>
</tr>
<tr>
<td>– high &gt;1.24 mmol/L (110 mg/dL)</td>
</tr>
<tr>
<td>– low</td>
</tr>
<tr>
<td>– absent</td>
</tr>
<tr>
<td>– usually present</td>
</tr>
<tr>
<td><strong>Pseudochylothorax:</strong></td>
</tr>
<tr>
<td>• Triglycerides</td>
</tr>
<tr>
<td>• Cholesterol</td>
</tr>
<tr>
<td>• Cholesterol crystals</td>
</tr>
<tr>
<td>• Chylomicrons</td>
</tr>
<tr>
<td>– low</td>
</tr>
<tr>
<td>– high &gt;5.18 mmol/L (200 mg/dL)</td>
</tr>
<tr>
<td>– often present</td>
</tr>
<tr>
<td>– absent</td>
</tr>
</tbody>
</table>

Table 6

<table>
<thead>
<tr>
<th>Causes of chylothorax and pseudochylothorax</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Chylothorax:</strong></td>
</tr>
<tr>
<td>• Trauma:</td>
</tr>
<tr>
<td>• Neoplasm:</td>
</tr>
<tr>
<td>• Miscellaneous:</td>
</tr>
<tr>
<td>• Idiopathic (about 10%)</td>
</tr>
<tr>
<td>thoracic surgery (especially if involving posterior mediastinum, for example, oesophagectomy), thoracic injuries</td>
</tr>
<tr>
<td>lymphoma or metastatic carcinoma</td>
</tr>
<tr>
<td>disorders of lymphatics (including lymphangioleiomyomatosis), tuberculosis, cirrhosis, obstruction of the central veins, chyloascites</td>
</tr>
<tr>
<td><strong>Pseudochylothorax:</strong></td>
</tr>
<tr>
<td>• Tuberculosis</td>
</tr>
<tr>
<td>• Rheumatoid arthritis</td>
</tr>
</tbody>
</table>
Guideline summary

Suspected pleural infection, non-purulent fluid – initial decision tree

Initial pH | Level of risk for CPPE / pleural infection | Initial action regarding drainage
---|---|---
≤ 7.2 | High risk | Insert ICD, assuming ultrasound demonstrates safe volume of accessible pleural fluid
> 7.2 to < 7.4 | Intermediate risk | Check LDH and review other parameters which may support CPPE / pleural infection. Consider ICD insertion if LDH > 900, especially if any of the following:
- Large pleural fluid volume
- Low pleural fluid glucose (72 mg/dL / ≤ 4.0 mmol/L)
- Pleural contrast enhancement on CT
- Septation on ultrasound
≥ 7.4 | Very low risk | No indication for immediate ICD

* Assuming ultrasound demonstrates safe volume of accessible pleural fluid.
† As evidenced by ongoing temperature, persisting elevation of inflammatory markers. Those with septations and pleural pH >7.4 should also be considered for drainage.

CPPE, complex parapneumonic effusion; LDH, lactate dehydrogenase; ICD, intercostal drain.
ICD, intercostal drain; TPA, tissue plasminogen activator; VATS, video-assisted thoracoscopy surgery.
Guideline summary

Malignant pleural effusion pathway

Confirmed diagnosis of malignant pleural effusion

Patient likely to benefit from intervention

YES

Fluid amenable to intervention

NO

Watchful waiting

NO

Best supportive care

YES

Lung considered re-expandable*

IPC

Therapeutic aspiration

NO

Ambulatory & extended pleurodesis strategy: IPC ± talc

Inpatient and early pleurodesis strategy
Chest tube and slurry or thoracoscopy and poudrage

YES

Non-draining and septated effusion – consider use of fibrinolytics

* Review of imaging, possible trial of benefit of aspiration before final decision.

IPC, indwelling pleural catheter.