| GUIDELINE | |
|---|---|
| **Pleural Empyema** | |
| **Scope (Staff):** | Medical, Nursing, ChAMP, Allied Health |
| **Scope (Area):** | PMH (PCH) |

**This document should be read in conjunction with this DISCLAIMER**

## Contents

## Aim

This guideline provides a clinical framework for the assessment, investigation and management of children and adolescents presenting to PMH/PCH with a pleural empyema.

## Definitions

**Pleural empyema** develops most commonly secondary to bacterial pneumonia.

**PPE:** Parapneumonic effusion;

- PPE and empyema represent a continuum from clear fluid with low white cell numbers to overt pus.
- A simple PPE may progress from the exudative stage with anechoic non-septated fluid (stage 1), through hyperechoic fluid with fibrinous septation (stage 2) to an organisational stage with hyperechoic loculations with or without thick pleural peel (stage 3).[1,2]

**VATS**: video-assisted thoracoscopic surgery.

## Background

There is no agreed standard treatment regimen for childhood empyema. Current literature suggests that there is no significant difference in outcomes between chest drain with intrapleural fibrinolytics or VATS. Chest drain and intrapleural fibrinolytics may offer the same clinical benefit but at a lower cost[1].

## Risk

Failure to follow this guideline may result in inappropriate clinical management.

## Key Points

- *Streptococcus pneumoniae* is the most common pathogen associated with pleural empyema[1-3]
- The possibility of PPE should be considered in all children with pneumonia.
- Chest X-ray (CXR) and chest ultrasound are the central radiological investigations
- *Routine* CT chest is not indicated, but should be considered if:
    - An infective cause is in doubt
    - Thoracotomy is being considered
    - There is complex disease
- Empiric intravenous antibiotics are the first line of treatment (see ChAMP guideline)
- If there is a moderate-large collection seen on ultrasound, chest drain insertion and intrapleural-fibrinolytic installation should be considered in conjunction with antibiotics.
- VATS should be reserved for failure of conservative management.

## Aetiology

- Most children and adolescents with empyema are previously healthy.[2]
- The most common pathogens in Australia are *Streptococcus pneumoniae* and *Staphylococcus aureus* (both methicillin susceptible *S.aureus* - MSSA and methicillin resistant *S.aureus* - MRSA).[2]
- Other organisms include Group A Streptococcus; *Streptococcus milleri* group, *Haemophilus influenzae*.
- Uncommon causes are *Mycoplasma pneumonia*, *Chlamydia pneumonia*, *Pseudomonas aeruginosa*, *Burkholderia pseudomallei* and Klebsiella species. In children at risk of aspiration, anaerobic organisms should be considered.
- *Mycobacterium tuberculosis* may present with pleural effusion with or without underlying lung changes.

## Management Overview (see quick guide in Appendix 1)

### *Initial investigations*

- CXR and chest ultrasound
- *Routine* CT chest is not indicated

### *Initial Treatment [1-4]*

- Empiric intravenous antibiotics are the first line of treatment.
- Chest drain insertion and intrapleural-fibrinolytic instillation should be considered as early as possible for moderate and large PPE.
- Small bore chest drain is as effective as a large bore chest drain.

### *Surgical Treatment*

- Any invasive procedure should be reserved for failure of conservative management[1, 3, 5, 6]
- There is no evidence that surgical intervention shortens speed of recovery. [7]
- Surgical interventions include video-assisted thoracoscopic surgery (VATS), mini-thoracotomy or open decortication.

### *Long Term Follow-up*

- CXR
- Lung Function

Most patients make a complete recovery. Management should aim to minimise short-term morbidity (e.g. pain, time to resolution of fever, length of hospital stay).

# DIAGNOSIS

## History

- Patients usually present with symptoms of pneumonia - cough, shortness of breath, fever, lethargy and chest or abdominal pain.
- In a patient with pneumonia, empyema should be considered where there is persisting fever or a lack of clinical improvement after 48 hours of antibiotics.

## Imaging

### Chest X-Ray

- Early signs include blunting of the costophrenic angle and a lateral rim of fluid around the lung. With large effusions there may be a complete 'white out' of the lung field making it impossible to differentiate between pleural fluid and consolidated lung; the presence of mediastinal shift away from the pathology supports the diagnosis of a pleural collection and ultrasound can differentiate non-invasively.
- Pleural thickening and underlying consolidation are frequently observed following treatment and, in isolation, do not mean failed therapy. CXR changes (particularly pleural thickening) may persist for 3–6 months following successful treatment.

### Chest Ultrasound

- Ultrasound is the central investigation in empyema. It is non-invasive, portable, and inexpensive and does not involve ionising radiation. It can differentiate pleural fluid from consolidated lung, demonstrate fibrinous strands within the fluid, assess loculation of fluid, estimate the size of effusion and guide chest drain placement.

### CT Chest

- Chest-CT does not provide benefit over ultrasound for determining the size and nature of PPE. Chest CT does provide information about parenchymal changes of the underlying lung. Chest CT is often useful if surgical intervention (e.g. decortication) is being considered.
- Chest CT is considered in cases where there is concern that infection is not the cause, particularly in those with late presenting empyema, blood stained pleural fluid or in a case that is not clinically improving despite appropriate treatment.[3]

## Blood Tests

- Full blood count (FBC) and C-reactive protein (CRP) should be performed;
  - Serial WCC and CRP are helpful for monitoring response to therapy.
  - A blood culture should be taken although the isolation rate is low (10 - 22%).
- Pneumococcal PCR can be considered on EDTA blood in children with empyema with negative blood cultures.[8]A Quantiferon-Gold assay may be of use if tuberculosis is likely on clinical and/or epidemiological grounds.

## Pleural Fluid

- In children with a moderate or large effusion, a sample of pleural fluid should be obtained as early as possible to identify the causative organism. In most instances, the sample can be obtained at the time of chest drain insertion.
- A fine needle aspiration of pleural fluid, obtained under ultrasound guidance, should be considered for children with a small effusion who are planned to be managed with antibiotics alone.
- Any pleural fluid that is available should undergo microbiological analysis including gram stain, culture and antibiotic sensitivity testing[9]. Fluid should also be sent for cytological analysis as malignant cells may be observed. A lymphocytosis may indicate tuberculosis or malignancy.
- Both pneumococcal antigen testing and pneumococcal PCR can be performed on pleural fluid and have high sensitivity and specificity.[3, 10, 11]
- In children with pleural effusions who are at risk of tuberculosis (birth or travel to high-incidence country, exposure to index case; symptoms for > 2 weeks), AFB stains, mycobacterial culture and PCR is recommended on pleural fluid.

### *Pleural fluid and other specimen collections:*

| Specimen | Tests required |
|---|---|
| **Pleural fluid x 3:**<br>1. Sterile yellow-top cytospin container<br>2. BACTECTM PEDS PLUSTM blood culture bottle (1-5ml)<br>3. An EDTA Blood Tube (1-3ml) | On each of the samples:<br>• Cell count<br>• Gram stain and culture<br>• *Pneumococcus* and *Staphylococcus aureus* PCR<br>• **AFB stain, mycobacterial culture and PCR |
| ±**Sputum** | • Microscopy, culture and sensitivity (MCS)<br>• ****Additional respiratory specimens for AFB stain and mycobacterial culture |
| ± **Nasopharyngeal aspirate** or throat swab | • Respiratory virus detection |
| ±****Blood** | • **Quantiferon-gold assay. |
| **If pleural tuberculosis is being considered (birth or travel to high-incidence country, exposure to index case or subacute presentation). Note that pleural TB can be paucibacillary resulting in negative AFB stain and culture.<br>**Isolation in a negative pressure room is required if tuberculosis is being considered. Airborne precautions must be taken at all times, with highest risk during aerosol generating procedures like intubation, obtaining induced sputums and aspiration of pleural fluid. | |

# MANAGEMENT

## Supportive Therapy

- Oxygen supplementation if hypoxic (oxygen saturation <93%),
- Fluid therapy
- Adequate analgesia
- Physiotherapy for assistance with early mobilisation only.

## Empiric Antibiotics

- Please also refer to ChAMP empiric guideline Acute Respiratory Tract Infection and ChAMP Medication Monographs
    - IV Ceftriaxone 50mg/kg (to a maximum of 2 grams/dose) 24 hourly

      AND
    - IV Vancomycin 15mg/kg (to a maximum initial dose of 750mg) 6 hourly (therapeutic drug monitoring is required)
- If there is a history suggestive of aspiration, add:
    - IV Clindamycin (10mg/kg/dose) 8 hourly to Ceftriaxone, instead of Vancomycin
- Revise antibiotics on the basis of microbiology results. Most empyema is caused by amoxicillin-susceptible organisms.

### *Special considerations;*

Discuss the following clinical situations with an Infectious Diseases physician or Clinical Microbiologist:

- **TB**: **Isolation in a negative pressure room is required if tuberculosis is being considered. Airborne precautions must be taken at all times, with highest risk during aerosol generating procedures like intubation, obtaining induced sputum sample and aspiration of pleural fluid.
- **For very ill children**: the addition of flucloxacillin should be considered.
- **Geographic risks**: If the child resides in the far north of Western Australia, consideration should be given to treating melioidosis (*Burkholderia pseudomallei*) or Acinetobacter infection, although *Streptococcus pneumoniae, Staphylococcus aureus* will still be the most likely pathogens.
- **Drug Allergy**: If there is a significant history of allergy to beta-lactams or vancomycin, alternative antibiotics will be required.

### *Review of empiric antibiotics*

- Antibiotics should be reviewed after microbiological results are available (blood culture, pleural culture and blood/pleural PCR) and with consideration of the child's clinical response.
- Most children can be treated with:

- IV benzylpenicillin: 60mg/kg/dose (to a maximum of 2.4g) 6 hourly and then,
- Oral amoxicillin: 30mg/kg/dose (to a maximum of 1g) three times daily
  - IV Ceftriaxone may be used if reduced susceptibility to penicillin is identified or to facilitate outpatient IV treatment.

- Children with proven Methicillin-sensitive *Staphylococcus aureus* empyema can be treated with:
  - IV flucloxacillin: 50mg/kg/dose (to a maximum of 2g), 6 hourly and then,
  - Oral cephalexin: 25mg/kg/dose (to a maximum of 1g) given 4 times daily.
  - Children with MRSA empyema should be discussed with an Infectious Diseases Physician or Clinical Microbiologist as sensitivity of individual pathogens vary.
- In children in whom no pathogen is identified, empiric intravenous therapy (IV Ceftriaxone and Vancomycin) should be maintained until clinical improvement.

  Amoxycillin/clavulanic acid (25mg/kg/dose of the amoxicillin component to a maximum of 875mg per dose given twice daily) is the preferred oral agent.

### *Duration of antibiotics*

- Fever can persist for several days. Children should receive IV antibiotics until afebrile for at least 24 hours.
- Consideration should be given to inserting a mid-line or PICC line at the same time as pleural drainage, to avoid issues with venous access. Refer to 'CVAD Indications, Referral, Booking and Insertion Guideline'.
- Oral antibiotics should be given after discharge for a period of 1-4 weeks, longer if necessary. The length of treatment depends on factors including the severity of the disease, causative organism and complications.

## Chest drain versus no chest drain

- Children with a small effusion and minimal respiratory distress usually respond to antibiotics alone, whereas those with a moderate to large sized pleural effusion and/or moderate-severe respiratory distress often require drainage.
- NOTE: Some children with a small pleural effusion, who are being appropriately managed with antibiotics alone, will progress to develop a moderate to large sized pleural effusion requiring drainage. If no clinical improvement at 48hrs and/or deterioration, repeat the CXR and chest ultrasound.

### *Intrapleural interventions*

- At PMH / PCH, chest drain plus fibrinolysis is the preferred option for children/adolescents with a pleural empyema requiring drainage, unless specific circumstances dictate otherwise.
  - Intrapleural interventions have been associated with significantly shorter hospital stays compared with intravenous antibiotics alone, while instillation of

intrapleural fibrinolytics offers benefit beyond simple chest tube drainage in shortening length of hospital stay.[1]

- There is no difference between (i) chest drain and fibrinolytic agents and (ii) surgical intervention, in terms of length of stay, duration of oxygen requirement, duration of fever, analgesia or treatment failure/adverse event rate.[1]

- Children with empyema who have a positive blood culture and/or require intensive care are at the highest risk for requiring repeat pleural drainage procedures.[12] Such children were successfully managed with repeat chest tube insertion rather than rescue VATS or thoracotomy in one study.[12] The treatment paradigm for empyema in children continues to shift toward the use of fibrinolytics. Early VATS is not necessary, and in many cases, rescue VATS can also be avoided.[12]

## *Chest Drain*

- A small pigtail catheter is preferred for chest drainage[20,21] and is inserted either in Paediatric Critical Care (PCC), Interventional Radiology or Theatre with appropriate analgesia and sedation or general anaesthesia.
- Once 10mLs/kg pleural fluid has been removed, clamp the drain to reduce the very small risk of re-expansion pulmonary oedema.[2, 13]
- The pigtail catheter should be aspirated 4 hourly or during periods of clinical concern – e.g. increased work of breathing, increasing oxygen requirement.
- There is no evidence that continuous Under Water Seal Drainage (UWSD) / ± suction of chest drains confers any advantage in treating empyema, however if UWSD is required the drain should remain clamped for one hour following initial drainage and following the instillation of fibrinolytics.
- Please refer to Chest Drain Management guideline in the Clinical Practice Manual.
- If the patient's clinical status deteriorates at any time (e.g. increased shortness of breath, chest pain, increasing oxygen requirement):
    1. Examine the patient,
    2. UNCLAMP drain if applicable,
    3. Attempt sterile aspiration of the chest drain;
    4. Consider an urgent portable CXR.

## *Fibrinolytics*

- Intrapleural Alteplase (tissue type plasminogen activator, tPA) should be instilled from the outset if the pleural fluid obtained is turbid or if there is evidence of loculations on ultrasound. [9,17]

*Dose:*

- For patients >10 kg, instil Alteplase 0.1mg/kg (maximum 6mg) in 1ml/kg 0.9% Sodium Chloride (maximum volume 50mls). Clamp the drain for 1 hour.[11,13] Give once daily for three days only.
- For patients <10 kg, instil Alteplase 0.1mg/kg in 10mls 0.9% Sodium Chloride. Clamp the drain for one hour.[11,13]

- Give once daily for 3 days only.

*Minor side effects*

- Transient chest pain during instillation and transient blood staining of the pleural fluid. For analgesia, intrapleural bupivicaine 0.25% can be instilled (0.5-1.0mL/kg) at the same time as tPA if significant discomfort [9].
- Rare cases of immediate hypersensitivity reaction and cases of bleeding have been reported in adults.

## Pain

- Pleuritic pain as well as the discomfort of a chest drain may reduce deep breathing and affect the child's willingness to cough. Adequate analgesia is essential to promote comfort and facilitate breathing exercises and mobilisation.

## Chest Drain Removal

- The ongoing requirement for the chest drain should be discussed on a daily basis with the treating medical team and documented in the patient's medical record.
- The timing of chest drain removal is a clinical decision. It may be useful to get a repeat ultrasound when nothing is draining to confirm the absence of a significant amount of fluid and to ensure the effusion is not loculated or the drain blocked.
- It is not necessary to await complete cessation of drainage. The chest drain can generally be removed if drainage is less than 1-2mL/kg/24h if the child has clinically improved.
- The chest drain should be removed briskly either:
  - while the child performs a Valsalva manoeuvre or
  - during expiration

  Refer to Chest Drain Management guideline for intercostal catheter removal procedure.

  Note: Some pigtail catheters require uncoiling prior to removal - ensure type of catheter is identified. See UreSil Pigtail Catheter Removal if this type of catheter is used.
- **There is no recommendation to complete a CXR as routine practice following uncomplicated chest drain removal**.[14, 15]
  - However, if the child shows respiratory distress after removal of the chest drain, complete an immediate clinical examination. If a pneumothorax is determined to be one of the differential diagnoses for the clinical signs after chest drain removal, then request a CXR and escalate care in accordance with escalation protocols.

## Discharge Planning and Follow-up

- Patients should be advised they must be followed up as an outpatient until they have fully recovered and their CXR has returned to normal; this can take up to 6 months.[9]
- All patients with suspected or confirmed TB will be managed by the infectious diseases team and followed up in the Anita Clayton Centre within 2 weeks of discharge.
- For other patients, an initial outpatient clinic review by the treating medical team should be scheduled for **six weeks** after discharge to complete:
    - A thorough physical examination, checking for catch-up growth, and no residual or new complications of the cardiorespiratory- and chest-wall musculoskeletal-systems.
    - Respiratory function testing and CXR
        - If there was significant infectious complications to the lung adjacent to the empyema at time of acute care.
        - If there is persistent reduced exercise tolerance and poor catch-up physical growth.
        - If there is persistent cough and/or chest pain
    - Routine immune function tests are not necessary, but may be considered in selected cases[9]. Immune studies should be completed if there is a past history of severe, recurrent and/or prolonged episodes of bacterial infection, prolonged and/or poor healing and recurrent boils and/ or abscesses, infection with an unusual pathogen, or infection with a pneumococcal vaccine serotype. Immune studies should be completed if there are persistent symptoms not resolved from the acute episode.
    - In young infants with a pleural empyema secondary to *Staphylococcus aureus* or *Pseudomonas aeruginosa* consider a sweat test to exclude cystic fibrosis.

| **Related internal policies, procedures and guidelines** |
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| Alteplase – Paediatric Monograph |
| ChAMP Paediatric Empiric Guidelines – Acute Respiratory Tract Infection |
| Chest Drain Management (Clinical Practice Manual) |

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# Appendix 1: Quick Guide to the treatment of Pleural Empyema