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# Plural Empyema Management in Children

## Link to Algorithm

### Introduction and Background

Pleural empyema is a relatively uncommon problem in general paediatrics, however recent studies have suggested the incidence of cases in children is rising (Strachan and Jaffe 2009). There are few randomised controlled trials or systematic reviews published in the literature on the management of pleural empyema in children. Two national guidelines from the UK and Australia published in recent years form the basis for this document (Balfour-Lynn, Abrahamson et al. 2005; Strachan and Jaffe 2011).

### The Hierarchy of Evidence:

The Hierarchy of evidence is based on the National Health and Medical Research Council (2000) and Oxford Centre for Evidence- based Medicine Levels of Evidence (May 2001)

**I** Evidence obtained from a systematic review of all relevant randomized control trials.

**II** Evidence obtained from at least one properly designed randomized control trial.

**III-1** Evidence obtained from well-designed pseudo-randomised controlled trials (alternative allocation or some other method).

**III-2** Evidence obtained from comparative studies (including systematic reviews of such studies) with concurrent controls and allocation not randomised, cohort studies, case control studies, or interrupted time series with a control group.

**II-3** Evidence obtained from comparative studies with historical control, two or more single–arm studies, or interrupted time series without a parallel control group.

**IV** Evidence obtained from case-series, either post-test or pre-test and post test.

**V** Expert opinion without critical appraisal, or based on physiology, bench research, or historically based clinical principles.

### Definition

Pleural Empyema is defined as the presence of pus (usually consisting of polymorphonuclear leucocytes and fibrin) in the pleural space. An empyema usually results as a complication of a parapneumonic pleural effusion and the current worldwide incidence ranges from 0.7 – 3.3 per 100,000 (Jaffe and Balfour-Lynn 2005; Strachan and Jaffe 2009). Generally pleural effusions and empyemas in childhood are secondary to acute bacterial infection, but can be as a result of uncommon infections such as pulmonary tuberculosis. Rarely, pleural effusions are the first

presentation of malignancy and this should be considered where the clinical presentation is atypical. If not treated correctly, pleural empyemas can result in significant morbidity in children including multiple surgical procedures and prolonged hospital admissions.

The disease process is a continuum but has been divided into three stages (Hamm and Light 1997) –

1. Exudative- in which a sterile exudate low in cellular count accumulates in the pleural space.

2. Fibrinopurulent- in which frank pus is present with an increase in white cells.

3. Organised- fibroblast proliferation leads to the formation of thick peel and potential lung entrapment, whereby the pleural space is characterised by a very thick exudate with heavy sediment.

## Aim

The management approach is guided by the staging of the pleural empyema but must be coupled with the clinical picture.

The aim of this guideline is to examine the evidence in the literature in order to provide a standardised pathway for the management of children presenting with pleural effusion/empyem. It is anticipated that this guideline will result in improved patient care and clinical outcomes. It is also envisaged that this document will eventually provide the framework for a national guideline to be rolled out at some time-point in the future.

## Diagnosis

**Clinical presentation:** Children often present with symptoms suggestive of pneumonia such as cough, fever and increased work of breathing. However many children present with atypical symptoms of upper abdominal pain, vomiting or general malaise. Pleuritic chest pain may develop. Physical examination reveals signs of respiratory distress such as tachypnoea, intercostal/subcostal recession, tracheal tug, nasal flaring and grunting. On auscultation of the chest, signs suggestive of a parapneumonic effusion include unilateral decreased chest expansion and breath sounds. Decreased tactile/vocal fremitus, dullness on percussion and scoliosis to the affected side are also prominent features of a parapneumonic effusion. **In a child with suspected bacterial pneumonia, if there is no improvement in the clinical presentation after 48 hours then a clinical suspicion of pleural effusion/empyema should be raised [V].**

## Investigations

### Imaging

### Chest X-ray (CXR)

A CXR should be performed routinely on all children with a raised clinical suspicion of pneumonia +/- parapneumonic effusion **[V].** An anteroposterior or posteroanterior film should suffice and there is no role for routine lateral CXRs **[V]**. Features on a CXR suggestive of a parapneumonic effusion include blunting of the costophrenic angle and a rim of fluid may be seen ascending the lateral chest wall on

the affected side. Increased opacification may often progress to complete "white out" of the entire lung field. Although, CXRs provide valuable information to the clinical picture, it is not possible to differentiate between a simple effusion and empyema by CXR alone (King and Thomson 2002). If a small pleural effusion is demonstrated on the initial CXR and there are no signs of clinical improvement within 48 hours, then a repeat CXR and a chest ultrasound should be requested **[V]**.

**Ultrasound**

Ultrasound is the investigation of choice for suspected pleural empyema. It is an informative, simple and non-invasive test, which should be performed on all children suspected of having a pleural effusion/empyema (Yang, Luh et al. 1992; Koh, Burke et al. 2002). The role of a chest ultrasound in the management of pleural effusion/empyema is to -

1. Differentiate between consolidation and pleural fluid
2. Estimate the size of the pleural effusion
3. Determine the echogenicity of the pleural effusion
4. Detect the presence of fibrinous septations in the pleural fluid
5. Provide guidance on the optimal chest drain insertion site, this site should be marked clearly at the time of ultrasound (Shankar, Gulati et al. 2000) **[III]**

Although it is a crucial diagnostic tool, it can be difficult to accurately stage a pleural empyema on chest ultrasound alone. If the empyema is significantly loculated and septated, then a chest drain insertion may not be a successful management option and further imaging may be required to determine this (Kunyoshi, Cataneo et al. 2006) **[V]**.

**CT**

A CT thorax should **not be used routinely** as an investigative tool in the management of pleural empyema (Jaffe, Calder et al. 2008) **[V]**. Although, CT is a superior radiological modality for examining the lung parenchyma and pleural space when compared with ultrasound, its role is limited in children due to the risks associated with radiation exposure and the requirement of sedation/general anaesthesia in younger children.

However, CT may have a role in more complicated cases that do not respond to initial treatment **[V]**. This is especially pertinent in those children with an atypical presentation or a background history of co-morbidities or where the diagnosis is uncertain. Also, although a CT is not usually required prior to chest drain insertion, a CT may be of benefit to determine the degree of residual empyema following chest drainage and / or fibrinolytic treatment and to identify whether there is an underlying lung abscess to decide whether decortication/debridement is warranted. It is the best method to differentiate peripheral lung abscess from empyema (Calder and Owens 2009). Therefore, it should only be reserved for such cases.

**Blood tests**

Baseline blood tests should always include a full blood count (FBC), C-reactive protein (CRP), pneumococcal PCR testing and blood cultures **[V]**. A raised white cell count (WCC) and neutrophil count along with a high CRP are often found at diagnosis. These tests are non-specific markers of inflammation and cannot be used to differentiate between bacterial and viral infections (Nohynek, Valkeila et al. 1995). However a decreasing WCC and CRP is often a sign that the patient is responding to treatment. As an adjunct to this, rising or static inflammatory markers may be indicative of an unresolving infection or abscess formation. ESR may be a useful measure in longstanding infection. Thrombocytosis is commonly seen in children who develop an empyema as part of the chronic inflammatory process involved. Usually, no intervention is necessary and it self resolves in time.

Urea and electrolytes should be performed at diagnosis to rule out either syndrome of inappropriate anti-diuretic hormone (SIADH) or haemolytic uraemic syndrome (HUS), two rare but serious complications which can occur in the clinical setting of a pleural empyema **[V]**.

A coagulation profile and a group and hold should be sent at diagnosis as part of a pre-operative screen for those children who may require chest drain insertion and intrapleural fibrinolytics. If a significant coagulopathy is present, then a haematology opinion may be warranted prior to any procedure being undertaken **[V]**.

Low serum albumin levels are often seen and rarely require treatment with albumin infusions. Serial blood tests are often not necessary and should be correlated with the clinical picture **[V]**.

**Airway sampling**

Sputum should be obtained and sent for culture and microscopy on all children old enough to produce sputum **[V]**. A nasopharyngeal aspirate for viral detection should also be sent on all children who present with corzyal symptoms **[V]**. If the child is intubated in PICU, a tracheal aspirate for culture and microscopy should be taken **[V]**. BAL should not be routinely performed on children presenting with an empyema **[V]**.

**Pleural fluid analysis**

Pleural fluid should be sent for cytology, culture and microscopy **[III]**. This should include staining for acid-fast bacilli and culture for mycobacterium tuberculosis and viruses. In order to increase the diagnostic yield from pleural fluid, samples should also be tested for PCR for streptococcus pneumoniae (Saglani, Harris et al. 2005; Wang, Kong et al. 2008). There is no role for routine biochemical analysis of pleural fluid in the clinical setting of an empyema in children unless the presentation or clinical course is atypical **[V]**.

## Management

### Referral

**Early** referral of **All** children with a suspected empyema to a respiratory paediatrician is essential **[V]**. The management of children with a suspected empyema, whether they are an in-patient in CHI or in a peripheral unit around the country, should be discussed with the respiratory paediatrician on call. All children clinically unwell and/or likely to require a chest drain should be transferred to CHI under the care of the respiratory team.

Any child requiring transfer to CHI should be medically stable for transport. On arrival to CHI, a surgical opinion from the cardiothoracic or paediatric surgical team is recommended in the majority of cases. Consultation with a paediatric intensivist should be sought if the child requires high dependency or intensive care.

### Supportive

Standard supportive and resuscitation measures should be implemented for all children. Oxygen supplemental therapy is recommended for all children with oxygen saturations <94%. Regular analgesia and antipyretics should be administered in order to keep the child comfortable. In particular, analgesia should not be held because of concerns of masking temperatures.

### Antibiotics

Intravenous (IV) antibiotics are indicated in all cases of empyema **[V]**. Hospital antibiotic guidelines recommend IV cefotaxime or ceftriaxone (high dose) in all uncomplicated cases. In addition, PO clarithromycin (dosage as per formulary) should be administered for seven days in total. IV clindamycin should be added in the setting of sepsis (i.e: bacteremia), multiple abscess formation, or a suboptimal response to standard antibiotic treatment and IV vancomycin reserved for those where there is clinical suspicion of MRSA infection. IV pipercillin-tazobactam should be reserved for children with a background of chronic lung disease, at high risk of aspiration or with a suspected hospital acquired infection. Once the offending organism is identified, antibiotics can be rationalised to counteract the specific organism **[II]**. IV antibiotics should be continued until the child is clinically improving, remains afebrile for at least 24 hours and/or the chest drain is removed **[V]**. A prolonged IV course may be considered in more complicated cases. If a prolonged course of IV antibiotics is expected, a peripherally inserted central catheter (PICC) or central venous catheter (CVC) line insertion should be considered at the time of chest drain insertion. The patient should be observed in hospital for at least 24 hours after switching from IV to PO antibiotics to ensure they tolerate the medication and that there is no relapse of the empyema **[V]**. In total, antibiotics (both IV and PO) should be administered for 3- 4 weeks, depending on the clinical course and the etiologic agent **[V]**. Occasionally, in complicated empyema, more prolonged courses may be required.

**Chest drain & fibrinolytics**

If a patient has a moderate to large pleural effusion in the setting of pneumonia then a chest drain should be considered both for diagnostic and therapeutic purposes **[V]**. Early drain insertion into a moderate to large effusion may allow for the complete resolution of the effusion. The instillation of urokinase to try to resolve early septated effusions and empyema may be necessary to allow for complete resolution (Sasse, Nguyen et al. 1997), and hence avoid a decortication. Where possible a minimally invasive drain inserted using the seldinger technique should be used to minimize post-op discomfort. Video-assisted thoracoscopic surgery (VATS) technique can be considered as an alternative treatment modality depending on the surgeon's level of expertise.

However, the clinical situation needs to be appraised prior to referral for chest drain insertion. An unwell child with an enlarging empyema and significant respiratory compromise should not be managed with antibiotics alone **[V]**. A conservative approach with antibiotics alone can be considered in children with an empyema who are systemically well with no respiratory compromise. The decision on the management approach rests with the treating respiratory paediatrician.

Prior to transfer to theatre for chest drain insertion, it should be ensured that the patient has the following available:

- Crossmatched for a unit of blood
- Any coagulopathy is corrected if possible, and blood products are available as dictated by the pre-op coagulation screen.
- The result of a urea and electrolytes sample taken within 24 hours is available to ensure no hyponatraemia or other electrolyte abnormalities.
- A CXR taken within 24 hours is available.
- Ultrasound assessment of the collection has been performed to determine degree of septation and volume of effusion to assess suitability for drain insertion. Ideally the site of optimal chest drain insertion should be indicated on the chest from ultrasound while the patient is lying with the unaffected side down as would be the position of the patient in theatre.
- Consent obtained for chest drain insertion +/- central line insertion +/- PICC line insertion.
- NPO for 6 hours

At the time of chest drain insertion, 5 samples of fluid should be sent for:

- Cytology
- Bacterial culture and microscopy
- Viral studies
- Staining for acid-fast bacilli and TB culture
- PCR for Pneumococcus

A chest x-ray is obtained in theatre under GA to assess drain position in case it needs to be readjusted and if there is still a residual collection despite drainage, then the first dose of urokinase can be given via the drain provided there is no air leak or bleeding. Oral paracetamol, Ibuprofen / Diclofenac should be prescribed and often oral morphine may be required in the first 24 to 48 hours. Good quality analgesia will ensure effective airway clearance, reduce anxiety and make clinical assessment easier. The drain is placed on 10cm$H_2O$ wall suction on the ward and chest physiotherapy is ordered. The volume of chest drainage is recorded every 12 hours and monitored for an air leak. It is important to check the drain daily to ensure it is not blocked.

**Fibrinolytics**

Intrapleural fibrinolytics have been shown to decrease the length of hospital stay in cases of complicated parapneumonic effusion or empyema **[II]**. They lyse fibrinous strands and clear lymphatic pores in the pleural space to encourage better drainage (Sonnappa and Jaffe 2007). Compared to VATS (video assisted thoracic surgery), there are variable outcomes reported, but most studies have small numbers. A study from Great Ormond Street Hospital of primary VATS vs. chest drain and fibrinolytics showed same length of hospital stay, same outcome, but a higher cost with VATS, suggesting no added advantage with VATS (Sonnappa, Cohen et al. 2006). Although there is no evidence that one fibrinolytic agent should be chosen over the others, urokinase is recommended as it is the only intrapleural fibrinolytic that has been studied in a randomised controlled trial in children **[II]**. The contra-indications to use of fibrinolytics include: bleeding from the drain, an air leak, and history of allergy to fibrinolytics. The first dose should be given in theatre after the intra-op CXR is reviewed, if there are no contra-indications.

***Equipment***

Dressing trolley, Dressing pack, Chlorhexidine / bethadine for cleaning, sterile gloves, 100ml bag of 0.9% saline, Urokinase, 50ml catheter tipped syringe, sterile scissors, Sterile drape, 2 sterile tubing clamps, 10ml syringe, green needle.

All patients should be given analgesia beforehand, oral morphine and oral midazolam for the first dose on the ward. After this if there was no significant discomfort then for further doses, analgesia only may be required.

***Procedure***

A sterile technique is used. Once gloved, the equipment is opened on the dressing pack.

Urokinase dosing (Thomson, Hull et al. 2002):

If the child is <10kg, then 10,000 units in 10mls saline

If the child is > 10 Kg, then 40,000 units in 40mls of normal saline

The urokinase solution is drawn up into a 50ml catheter tip syringe.

The chest drain tubing and connection to the underwater seal is painted and then placed on a sterile drape. The tube is then clamped above and below the chest drain connection and the underwater

seal is disconnected from the chest drain. The catheter tip syringe is then connected to the chest drain, the clamp removed and the urokinase slowly pushed into the drain and the drain then reclamped, and connected to the underwater seal with the clamp still on. Of note, this is the only circumstance in the management of pleural empyema where a chest drain should be clamped. The urokinase is left in the drain and pleural space for 4 hours and the drain is then unclamped and wall suction applied to the underwater seal. The child needs 30-minute observations to ensure no increased work of breathing, desaturation, or the development of subcutaneous emphysema. If any clinical concerns arise, the cardiothoracic or paediatric surgical team involved should be contacted immediately. As an alternative to clamping of the chest drain, elevating the tube in a loop (generally only 30cm of an elevated loop is required) so that gravity holds in the fluid may be considered. A CXR should be performed prior to and post removal of a chest drain or as clinically indicated.
The urokinase is instilled twice a day for 3 days, i.e. 6 doses (Thomson, Hull et al. 2002). After this there is no role for further fibrinolytic treatment **[II]**.

**Surgery**

In a meta-analysis comparing the results of primary decortication and non-operative intervention including a chest drain for paediatric empyema, decortication was associated with a lower mortality rate, lower re-intervention rate, shorter length of hospitalisation, decreased time with a chest tube and shorter course of antibiotic therapy (Avansino, Goldman et al. 2005). However, in most patient's, treatment with a chest drain and fibrinolytics produces the same outcome as decortication without the need for a larger scar and usually less pain involved. Although the radiological improvement is more rapid with open decortication, at follow-up months later there is often no difference compared to those treated with chest tube drainage and fibrinolytics **[V]**. Therefore open decortication is reserved for those who fail treatment with chest drainage, fibrinolytics and antibiotics **[V]** i.e.:

- Rising WCC and / or CRP and / or pyrexia despite a course of fibrinolytic treatment, in the absence of another cause for the sepsis, i.e. lung abscess, line infection, UTI, concomitant viral infection.
- Worsening CXR appearance or failure to resolve a large pleural collection.
- An empyema complicated by a large air leak with pneumothorax or subcutaneous emphysema, as fibrinolytics are contra-indicated.
- Occasionally, a child will present with a well-developed empyema with multiple loculations and very little liquid component. In that case a primary decortication may be considered.

Prior to surgery a CT scan is often needed to assess for the presence of an underlying lung abscess and to quantify the amount of empyema remaining, as if there is very little residual empyema and a lung abscess is the cause for ongoing sepsis or X-ray changes, then persisting with intravenous antibiotic therapy for a longer period may be warranted instead of surgery.
At surgery, a mini-thoracotomy is generally used, although a VATS is an acceptable alternative depending on local surgical expertise. All empyema is removed and careful attention to peel the rind

off the chest wall and lung to ensure full expansion of the lung by the end of surgery. Lung abscesses can also be unroofed and debrided to aid faster resolution, with attention to try to avoid lung resection. Post-operatively, CXR is required as clinically indicated, chest physiotherapy to encourage lung volume recruitment, and early mobilisation.

## Follow-up

A follow up review with a CXR should be performed within one week of discharge **[V]** and the patient reviewed at the cardiothoracic or paediatric surgical clinic. A respiratory review should be arranged for 6 months following discharge at which time an x-ray should be performed. This is to ensure complete resolution of clinical symptoms and ensure normalisation of imaging. Children may need to be seen sooner in addition if clinically indicated. Most CXR changes resolve within three to six months (Sonnappa, Cohen et al. 2006). An immune work up is not necessary in a previously well child with no history of recurrent infections **[V]**. A sweat test to rule out cystic fibrosis should be performed if the infecting organism is either staphylococcus aureus or pseudomonas aeruginosa (Bush 1994) **[V]**.

Link to References