



## Paediatric Empyema Thoracis: Recommendations for Management

### Position statement from the Thoracic Society of Australia and New Zealand.

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## **Conflicts of Interest Declaration**

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## ABSTRACT

- Empyema is an uncommon complication of pneumonia and is an accumulation of infected fluid in the pleural space.
- All children with empyema should be managed in a hospital with appropriate paediatric expertise preferably under the care of a Respiratory paediatrician as treatment of paediatric empyema is very different to that of adult disease.
- An antero-posterior/posterior-anterior chest X-ray should be performed in all children in whom empyema is suspected; there is no need for a routine lateral film.
- An ultrasound should be performed on all children with empyema as it is the best technique to differentiate pleural fluid and consolidation, estimate effusion size and grade complexity, demonstrate the presence of fibrinous septations and guide chest drain placement.
- A routine pre-operative CT should not be performed and should be reserved for complicated cases where children have failed to respond to treatment or if there is concern that there is other pathology such as a tumour.
- All children with empyema should receive high dose antibiotic therapy via the intravenous route to ensure pleural penetration.
- Appropriate antibiotics should be used to cover at least *Streptococcus pneumoniae* and *Staphylococcus aureus*.
- Moderate to large effusions require drainage.
- Chest drainage alone is not recommended and the intervention of choice is either percutaneous small bore drainage with urokinase or video-assisted thoracoscopic surgery.

- Oral antibiotics should be given for between 1 and 6 weeks duration following discharge.

## **Development of the document**

This position statement was developed by the working party comprising the principal investigators from the Australian Research Network in Empyema (ARNiE) and a representative from New Zealand (JT), and chaired by Adam Jaffe. The paediatric community of the Thoracic Society of Australia and New Zealand (TSANZ) were consulted on several occasions for their feedback and it was also made available to the wider TSANZ membership for comment. Consensus on the document was reached at a workshop at the TSANZ Annual Scientific Committee 2010. It has been endorsed by the Executive and the Clinical Care and Resources Standing Subcommittee of the TSANZ.

The recommendations were developed after examining evidence from English language publications searched using Medline with key words ‘pleural empyema’, ‘parapneumonic effusion’, and ‘children’, over years 1960-2009.

A total of 242 articles were identified, with 192 publications of relevance considered dating back to 1991.

The quality of evidence and levels of recommendations in this paper are based on the Grading of Recommendations Assessment Development and Evaluation (GRADE) [1-3]. Briefly a ‘Strong’ recommendation is one in which most patients and clinicians would want this recommendation. For ‘weak’ recommendations, clinicians recognise different choices and the need to help patients make a choice and that most patients would want the recommendation, though recognising that many would not. ‘No specific recommendation’ indicates that the advantages and disadvantages are similar [1]. In addition, the GRADE recommendation classifies the quality of evidence as: ‘High’ quality evidence where further research is unlikely to change our confidence in the estimate of effect; ‘Moderate’ quality evidence where further research is likely to

have an impact on our confidence in the estimate of effect and change the estimate; ‘Low’ quality evidence where further research is very likely to have an impact on our confidence in the estimate of effect and change the estimate; ‘Very low’ quality evidence where any estimate effect is very certain [3]. We have include ‘NO’ evidence if none exists.

## **INTRODUCTION**

Empyema is an uncommon complication of childhood pneumonia and general paediatricians may only see a few cases in their career [4]. Although mortality rates in paediatric empyema are very low, empyema causes significant morbidity including substantial health care costs and burden of care. Many treatment options are available, however due to a lack of quality research there is limited high grade evidence to direct best standards of care. In an attempt to address this, the British Thoracic Society published guidelines in 2005 [5] but there are no local Australasian guidelines. The need for local guidelines was highlighted in a recent survey of the management practices in all Australian hospitals with paediatric beds [4]. This survey demonstrated a wide range of treatments were practised in these hospitals suggesting a lack of consensus in the management of paediatric empyema in Australia. Furthermore, the study also demonstrated that paediatric empyemas are occasionally treated in smaller rural hospitals without paediatric specialists. Thus the PRMG of TSANZ realised the need to develop local guidelines to aid general paediatricians and other physicians managing children with empyema in the community in Australia and New Zealand.

## **EPIDEMIOLOGY**

Childhood empyema occurs in 0.7% of pneumonias in Australia; with a reported incidence of 0.7- 3.3 per 100,000 worldwide [4;6]. Recent studies in countries such as USA, Canada, Spain, France, Scotland and England have suggested that the number of cases of childhood empyema have been increasing. The cause for this is unclear but a number of reasons have been postulated, including a decrease in antibiotic use in primary care. Another suggestion has been that the rise is related to the introduction of the 7-valent pneumococcal vaccine (7v PVC) into national immunisation programs which has led to an increase in invasive pneumococcal empyema disease caused by non-vaccine serotypes [7-18]. This view is in contrast to a number of studies throughout the world, including Australia, which have shown an increase in the prevalence of empyema prior to the introduction of the 7v PVC [4;19-21].

A recent study by the Australian Research Network in Empyema (ARNiE) demonstrated that the majority of infections associated with empyema were caused by *Streptococcus pneumoniae* and the majority of the pneumococcal serotypes were non 7v PVC vaccine related, in particular serotypes 1, 3 and 19A [22]. Irrespective of the cause, it is likely that general paediatricians will see more cases in the future.

Fortunately children rarely die from empyema, unlike adults where mortality is as high as 20% [23]; however the burden of empyema on healthcare resources is substantial [24-26]. Epidemiological paediatric empyema studies have established that empyema has significantly greater morbidity compared to community acquired pneumonia as it is more likely to require intervention, result in prolonged hospital stay and antibiotic use, and patients are likely to require more intensive management.

## **PATHOPHYSIOLOGY**

The pleural space usually contains a small amount of fluid (0.3ml/kg of body weight), which is absorbed and secreted in equilibrium via the lymphatic drainage system. This circulatory system can cope with a substantial increase in fluid production; however disruption of this balance can lead to fluid accumulation and an associated pleural effusion, which may be further exacerbated if infection is present. Infection in the lung activates an immune response and stimulates pleural inflammation. Pleural vasculature becomes more permeable and inflammatory cells and bacteria leak into the pleural space causing pleural fluid infection and formation of pus resulting in the classical empyema. This influx is mediated by pro-inflammatory cytokines such as tumour necrosis factor, interleukin (IL)-1 $\beta$  and IL-6 secreted from mesothelial cells [27-29]. The activation of the coagulation cascade and disruption of enzymes of the fibrinolytic system such as tissue type plasminogen activator and plasminogen activator inhibitor type 1 (PAI-1), which are responsible for fibrin balance, results in fibrin deposition and blockage of lymphatic pores leading to further accumulation of fluid.

It is unknown why some healthy children develop empyema. Several studies have identified possible genetic determinants for predisposition to invasive pneumococcal infection [30-32]. It is possible that future genetic studies will identify which children are at risk of developing invasive bacterial disease.

## **DEFINITION**

Pneumonic infection and the associated inflammation of the pleural lining leads to an exudative uncomplicated parapneumonic pleural effusion. This effusion becomes

complicated if there is invasion of the pleural space by bacteria [33]. The term ‘empyema’ is derived from the Greek words *pyon*, meaning pus and *empyein*, meaning pus-producing. Thus by definition the presence of pus in the pleural space is consistent with the diagnosis of empyema.

While this disease evolves in a continuum, it has been divided into 3 distinct stages by the American Thoracic Society [34]:

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.

## **CLINICAL PRESENTATION AND EXAMINATION**

Children with empyema present in a similar fashion to those with pneumonia. Initially fever, malaise, tachypnoea are the presenting signs. Cough may be absent in the early part of the pneumonic process caused by *Streptococcus pneumoniae* but develops as the disease advances. Chest pain and diarrhoea may be a feature. Children often lie on the affected side to minimise pain and to improve ventilation and perfusion matching. They may have a scoliosis to the affected side. Chest examination typically reveals decreased unilateral chest expansion with reduced breath sounds on auscultation. Whispered pectoriloquy and tactile fremitus are increased in pneumonia and, following the development of pleural fluid, these decrease with an associated stony dull percussion. Typically, a persistent fever despite 48 hours of appropriate antibiotic

treatment, together with a change in physical signs should alert the clinician to the possible development of pleural fluid as a complication of pneumonia.

### **CLINICAL HISTORY POINTS**

Risk factors should be determined on admission, and may include a history of chronic illness, congenital or chromosomal abnormality, anatomic or functional asplenia, immuno-compromise, previous invasive pneumococcal disease (IPD), childcare attendance, vaccination status, prematurity and parental smoking history. Knowledge of the geographical area and indigenous status in which a child lives is important to guide antibiotic treatment as some bacteria, e.g. MRSA are a more common cause of community acquired pneumonia in certain communities. If there is a history of recurrent infections in the child, then consideration should be given to doing basic immunological investigations including immunoglobulin (Ig) G, IgM, IgA, IgE subclasses, T cell subsets and vaccine responses.

### **INVESTIGATIONS**

**Imaging** – the aim of imaging is to determine the presence of fluid, differentiate a simple parapneumonic effusion from an empyema and assess the complexity of the latter.

#### **a) Chest X-ray (CXR)**

While a CXR is not routinely recommended in children with a mild uncomplicated lower respiratory tract infection [35], CXR should be performed in children presenting with moderate to severe respiratory distress or if there are localised signs. Anterior- posterior or posterior-anterior films will demonstrate blunting of the costophrenic angle and pleural shadowing in more advanced disease; however it is not

possible to differentiate fluid from pleural thickening and is not useful to stage the disease. In some cases there may be complete ‘white out’ of an affected lung. Mediastinal shift away from the affected side suggests the presence of fluid and a shift towards the affected side indicates collapse. A CXR may commonly demonstrate a scoliosis in children with empyema but this usually resolves spontaneously and does not require treatment [36]. There is no role for a routine lateral CXR due to increased radiation exposure as it does not provide additional useful information. A lateral decubitus or erect film may be used to differentiate a simple parapneumonic effusion from an empyema if ultrasound is not available [37]. It is the consensus that additional X-rays are not required as the mobility of the fluid can be determined with ultrasound without the need for additional radiation exposure if this facility is available [38]. Furthermore, daily X-rays are not necessary to monitor progress as changes on CXR lag behind clinical status and are likely to be abnormal despite complete clinical resolution, even after 6 months [25].

## **b) Ultrasound**

Ultrasound is the central investigation in the management of paediatric empyema. It is non-invasive, does not use ionising radiation and provides a dynamic assessment of the chest and is readily repeatable. Furthermore, it is cheap, easy to perform, and is able to differentiate pleural fluid from consolidation. The size of the effusion can be estimated and guidance provided for the best spot for chest drain placement.

Ultrasound is also able to demonstrate the presence of fibrinous septations within pleural collections and stage the complexity of the empyema [39-44], although to a certain extent accurate interpretation relies on adequate knowledge and experience of

pleural ultrasonography in children and it may not be readily available in smaller rural hospitals. Ultrasound grading is unhelpful in predicting clinical outcome [42].

### **c) Computerised Tomography (CT)**

Chest CT scans have the advantage in that they are able to demonstrate underlying parenchymal abnormalities better than CXRs [42]. Many surgeons request a routine CT scan for use as a 'road map' when performing minimally invasive endoscopic surgery where direct visual access is limited. This helps plan the placement of instruments in order to decrease risk and avoid potential complications such as broncho-pleural fistula, which may result from puncturing lung parenchyma in close proximity to the pleura. However, this is not the routine practice of all surgeons [37]. The disadvantages of chest CT is that it often requires general anaesthesia or sedation in a young uncooperative child and exposes the child to relatively larger doses of radiation. It is unable to detect the presence of fibrinous septations, which are usually too thin and of insufficient density to identify and thus is not better than ultrasound in staging the complexity of the disease [41;44]. Furthermore, routine CT scans are not useful in predicting clinical outcome [42]. CT scans should not be done routinely in children with empyema, however they have a role in complicated cases if a child fails to respond to treatment and there is concern that an abscess has developed or, if the presentation is atypical and there are concerns that the child may have other pathology such as a tumour.

### **d) Ventilation-perfusion (VQ) scans**

The limitation of the above modalities is that they demonstrate structure rather than function. VQ scans are relatively simple to perform and can be abnormal in children

up to 10 years after empyema [45]. There is no role for a VQ scan in the acute management of empyema. Furthermore, a recent report demonstrated that patients are not agreeable to having the investigation performed at follow up when they have clinically recovered. In those that had the investigation, the majority had normal scans 6 months following the empyema [46].

### **Imaging Recommendations:**

- An AP or PA chest X-ray should be performed in all children in whom an empyema is suspected. [STRONG Recommendation, HIGH QUALITY Evidence]
- There is no need for daily ‘routine’ CXRs. [STRONG Recommendation, NO Evidence]
- There is no need for a routine lateral or lateral decubitus CXR, but the latter is an alternative if ultrasound is not available. [STRONG Recommendation, NO Evidence]
- Ultrasound is the investigation of choice and should be performed on all children with suspected empyema. [STRONG Recommendation, HIGH QUALITY Evidence]
- A routine pre-operative CT should not be performed. [STRONG Recommendation, MODERATE QUALITY Evidence]
- A CT should be reserved for complicated cases, where a child has failed to respond to treatment, or there is concern that there is other pathology. [STRONG Recommendation, LOW QUALITY Evidence]
- There is no role for VQ scans in the management of paediatric empyema. [STRONG Recommendation, MODERATE QUALITY Evidence]

## **Blood Tests**

Blood tests may help confirm the diagnosis and aid monitoring the progress of the disease. It is generally a good principle to limit blood testing in children as it is invasive and associated with discomfort. Consideration should be given as to whether the benefit of any test outweighs the risks.

### **a) Microbiology**

The yield of isolating causative bacteria from blood cultures is low, probably due to prior antibiotic use. However, the identification of causative bacteria helps to rationalise antibiotic choice and so all children should have initial blood sent for culture. If available, it is worth sending for molecular techniques to detect organisms in culture negative cases.

### **b) Full blood count**

White blood cells (WBC), particularly neutrophils, are raised at initial presentation and return to normal once the pleural space and lung parenchyma are sterilised. However this test cannot differentiate bacterial from viral infections. There is no role for routine WBC testing to monitor disease as the reduction of fever pattern is the most useful sign to indicate disease improvement. However, in cases where fever persists despite perceived adequate treatment, a persistent elevated WBC raises suspicion of abscess formation or inappropriate antibiotic cover. Similarly, a decreasing WBC is reassuring that the infection is being treated appropriately. The C-reactive protein acts in the same way as WBC. A falling C-reactive protein is usually reassuring, indicating that the child is getting better and a persistently raised CRP indicates an ongoing infective process. It should not be done routinely as emphasis should be placed on the clinical condition of the child, with particular regard to

pattern of fever. It is recommended that a full blood count and C-reactive protein be sent when cannulating the child at the beginning of intravenous antibiotic treatment in order to have a baseline in case investigations are needed at a later date.

Thrombocytosis is common due to chronic inflammation in empyema. There is no role for aspirin. Low platelets, together with anaemia should raise suspicion of haemolytic uraemic syndrome, which is a reported complication of empyema caused by release of neuraminidase by *Streptococcus pneumoniae*. Clinically, this complication may present with pallor, petechiae and oliguria [47].

### **c) Coagulation studies**

In some cases surgeons request a preoperative clotting screen. However in previously well children clotting is usually normal [48]. Despite the theoretical risk of fibrinolytics affecting clotting, there have only been two reported cases of bleeding associated with pleural instillation of fibrinolytics in childhood empyema [49;50]. A life threatening haemothorax as a result of instillation of fibrinolytics has been reported in a baby [49], but in this case the dose of urokinase was 5 times that used in subsequent studies with no reported adverse events [25;51-52]. Again, blood for baseline preoperative coagulation studies should be requested at the time of initial cannulation but there is no role for repeated measures.

### **d) Electrolytes, urea and creatinine (EUC)**

All children should have EUC performed at initial cannulation to ensure that they have not developed the syndrome of inappropriate anti-diuretic hormone (SIADH) or haemolytic uraemic syndrome. There is no need for routine monitoring of EUC's.

### **e) Albumin**

Serum albumin is often low and there is no role for routine albumin infusions in usual circumstances. Albumin levels normally recover spontaneously. Occasionally

children require albumin infusions if they develop gross peripheral oedema. This is rare.

**Table 1 Indication for blood tests**

<b>Blood Test</b>	<b>When recommended</b>	<b>Result</b>	<b>When repeated</b>
Culture (and bacteriological molecular tests if available)	At baseline	Culture often negative	If disease is unresponsive to treatment or complication developing
White Blood Cells C-reactive protein	At baseline	<b>Normal</b> suggests other non infective pathology <b>High</b> confirms infective process.	If disease is unresponsive to treatment or complication developing
Haemoglobin	At baseline	<b>Low</b> suggests HUS or chronic disease	If concerns that HUS developing
Platelets	At baseline	<b>Low</b> suggests haemolytic uraemic syndrome <b>High</b> suggests inflammatory response	If concerns that HUS developing
Coagulation	At baseline (optional)	Usually normal	Not required
EUC	At baseline	<b>Low</b> sodium suggests SIADH <b>High</b> urea and creatinine suggests HUS	If concerns that SIADH or HUS developing
Albumin	Not recommended	Often low	If peripheral oedema develops

**Recommendations:**

- Blood should be sent for culture and for enhanced molecular testing (if available).

[STRONG Recommendation, HIGH QUALITY Evidence]

- WBC count and C-reactive protein should be done on initial cannulation. There is no role for routine repeat testing which should be reserved for cases where there is persistent fever and there is concern that a patient is not responding to appropriate therapy. A decreased WBC and C-reactive protein is reassuring in these circumstances. [STRONG Recommendation, NO Evidence]
- There is no role for aspirin in thrombocytosis in children. [WEAK Recommendation, NO Evidence]
- Consideration should be given to sending preoperative coagulation studies with initial blood investigations prior to surgery, but there is no need for repeat testing. [WEAK Recommendation, NO Evidence]
- EUC should be done on admission and only repeated if there is a need to monitor response to treatment of electrolyte abnormalities or there is concern that HUS is a complication. [STRONG Recommendation, LOW QUALITY EVIDENCE Evidence]
- There is no role for routine albumin infusions to correct low serum albumin. [WEAK Recommendation, NO Evidence]

## **Pleural Fluid Investigations**

### **a) Biochemistry**

While it is routine to perform a diagnostic pleural tap and utilise biochemical markers to guide management in adults, it is not recommended in children as it requires cooperation or sedation and is painful. Therefore pleural fluid investigations can only be undertaken if the empyema requires drainage as part of therapy.

The presence of pus cells in pleural fluid, together with a high albumin and lactate dehydrogenase (LDH) supports the diagnosis of empyema however there are limited

data to support the use of biochemical markers to guide therapy in children. A lymphocytosis should raise suspicion of a malignancy or tuberculosis.

#### **b) Microbiology**

All pleural fluid should be sent for culture and microscopy. The reported rate of identifying an infectious organism from pleural fluid by standard culture varies from 8% - 76%, which is likely to reflect prior antibiotic treatment [5;6]. Ideally, specific and broad range polymerase chain reactions (PCR) such as 16sPCR should be done if available to increase the chances of detecting bacteria and help rationalise antibiotic therapy [53-57]. In some laboratories 16sPCR results are available within 48 hours and so are clinically useful if that service is available.

#### **Pleural fluid recommendations:**

- Diagnostic thoracentesis in children should not be performed. If there is a need to access the pleural cavity then consideration should be given to the placement of a drain, thus ensuring the child undergoes only one invasive intervention. [STRONG Recommendation, HIGH QUALITY Evidence]
- Pleural fluid should be sent for cytology, microscopy and culture, including for *Mycobacterium tuberculosis*. [STRONG Recommendation, HIGH QUALITY Evidence]
- Ideally, pleural fluid should be tested using enhanced molecular techniques such as PCR. [STRONG Recommendation, HIGH QUALITY Evidence]
- There is currently no role for pleural biochemical markers to guide therapy in children. [WEAK Recommendation, LOW QUALITY Evidence]

- Pleural fluid should be examined for the presence of white cells and bacteria on microscopy to support the diagnosis of empyema. [STRONG Recommendation, HIGH QUALITY Evidence]

## **MANAGEMENT**

Regardless of which treatment is used in empyema, the outcome for children is generally excellent. The aim of treatment is to resolve clinical symptoms and prevent further progression of empyema, sterilise the pleural cavity, reduce fever, shorten hospital stay and re-expand the lung with return to normal function. This often requires fluid drainage. It is recommended that all children with empyema be managed by, or in consultation with, respiratory paediatricians in conjunction with paediatric surgeons. This means that, if feasible, children should be transferred to a tertiary paediatric centre.

### **a) Supportive therapy**

Children should have supplemental oxygen if their saturations are below 93%. Other standard therapy includes fluid replacement, antipyretics and analgesia. There is no role for chest physiotherapy apart from early mobilisation and encouragement of deep breathing and coughing, particularly after surgical intervention or tube drainage. In order to achieve a more rapid disease resolution and rehabilitation, it is important to ensure that the child receives adequate analgesia to allow pain free respiration and mobilisation.

### **Recommendations:**

- Pulse oximetry is necessary to assess oxygenation. [STRONG Recommendation, HIGH QUALITY Evidence]
- Supportive therapy includes supplemental oxygen, antipyretics and attention to hydration and fluid balance. [STRONG Recommendation, NO Evidence]
- Children should receive adequate analgesia. [STRONG Recommendation, HIGH QUALITY Evidence]
- There is no role for routine physiotherapy apart from encouraging mobilisation after intervention. [STRONG Recommendation, LOW QUALITY Evidence]
- Ideally all children with empyema should be managed by, or in consultation with, respiratory paediatricians in conjunction with paediatric surgeons. If feasible, children should be transferred to a tertiary paediatric centre. [STRONG Recommendation, LOW QUALITY Evidence]

#### **b) Antibiotics**

All children with empyema will need antibiotic therapy and it is important to ensure pleural penetration and thus high doses via the intravenous route in the early stages of the disease are recommended. Initially in the absence of a positive culture the choice is dependent on local bacterial causes of community acquired pneumonia and local antibiotic policy will vary. The recent ARNiE study into the bacterial causes of empyema in children in Australia used enhanced molecular techniques: the commonest organisms were *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Staphylococcus aureus* and MRSA. It is recommended that the choice of antibiotics adheres to the local hospital infection control policy on management of community acquired pneumonia. Antibiotic choice can be rationalised if the organism is subsequently identified. It is recommended that the initial empirical choice of antibiotics should cover at least *Streptococcus pneumoniae* and *Staphylococcus*

*aureus*. Intravenous benzylpenicillin is a cheap and excellent drug in the majority of cases but has limited cover against *Staphylococcus aureus* and so the addition of flucloxacillin is recommended. Other alternatives include co-amoxiclav or a cephalosporin, such as cefotaxime or ceftriaxone, with the addition of flucloxacillin. Community acquired MRSA is commoner in some Indigenous communities and some hospitals use lincomycin or clindamycin as the first choice of antibiotic for the treatment of a complicated community acquired pneumonia. The presence of pneumatoceles on CXR raises the suspicion of *Staphylococcus aureus* as the causative organism, though they are also seen in Pneumococcal disease. Anaerobic infection should be considered in those children at risk of aspiration. There is no need to routinely use a macrolide antibiotic but its use should be considered in any child in whom *Mycoplasma pneumoniae* is thought to be the cause. However, *Mycoplasma pneumoniae* vary rarely causes empyema in children, particularly in the under 5 year old population.

Once a the child has been afebrile for 24 hours then consideration can be given to changing from intravenous to oral antibiotics. The choice of oral antibiotic is dependent on the organism identified (if any) or the class of antibiotic used successfully intravenously. Common choices include co-amoxiclav or a cephalosporin. It is recommended that children should be on at least 7 days but some physicians use up to 6 weeks of oral therapy. There is no consensus of the length of treatment which usually is dependent on the severity of the disease, the length of stay in hospital, complications and causative organism.

### **Recommendations:**

- Initial antibiotics should be high dose and intravenous to ensure adequate pleural penetration. [STRONG Recommendation, HIGH QUALITY Evidence]
- Empirical antibiotic treatment must ensure *Streptococcus pneumoniae* and *Staphylococcus aureus* cover. [STRONG Recommendation, HIGH QUALITY Evidence]
- Consideration should be given to coverage of MRSA if a child comes from a community with a high prevalence of MRSA. [STRONG Recommendation, HIGH QUALITY Evidence]
- Macrolides should be used when *Mycoplasma pneumoniae* is thought to be the causative organism but should not be used routinely.[WEAK Recommendation, MODERATE QUALITY Evidence]
- Intravenous antibiotics can be changed to oral antibiotics once a child has been afebrile for 24 hours. [WEAK Recommendation, NO Evidence]
- There is no consensus on the length of oral antibiotic treatment which varies from at least 1 week to 6 weeks. [WEAK Recommendation, NO Evidence]

### **Indications for pleural cavity drainage**

The decision to intervene with drainage is easy in a child with moderate to severe respiratory distress, a large pleural effusion and ongoing sepsis. The decision is much more difficult in those early on in the disease with mild respiratory distress and a small effusion because some parapneumonic effusions and early empyemas may resolve spontaneously and it is impossible to predict which child will progress to a more complicated empyema. The timing of pleural cavity drainage interventions is driven by each individual clinical case, local expertise and is a balance of watching and waiting to see if there is spontaneous improvement or the need for invasive

therapy. It is recommended that in those cases where there is little local medical expertise children are transferred early. Importantly, as the outcome in nearly all instances is excellent, the only disadvantage of waiting in a child with a small effusion is a prolonged length of stay in hospital.

### **Drainage of pleural fluid**

Drainage is an essential component in the treatment of large pleural effusions, and is necessary for establishing re-expansion of the lung. There are many literature reviews, case series and retrospective studies but only five randomised controlled clinical trials have been published to guide a consensus on best intervention [25;26;52;58;59].

Comparisons between studies are difficult as all use different protocols, dosing regimens for fibrinolytics and outcome measures.

### **Intervention options**

The options available for definitive drainage are: chest drain insertion alone or with instillation of fibrinolytics; video assisted thoracoscopic surgery (VATS) and open thoracotomy. When chest drains are used alone patients do make a complete recovery, however the length of stay is prolonged (ranging from 5 to more than 29 days) compared to other interventions, with associated health cost implications [60-62]. Furthermore, patients often require rescue surgical treatment [63]. The use of chest drains alone is not recommended.

The instillation of intrapleural fibrinolytics such as urokinase or tissue plasminogen activator (alteplase) through chest drains shortens hospital stay when compared with chest drain usage alone. It is thought that fibrinolytics act by breaking down fibrin

bands which cause loculation of the empyema thus improving drainage of the infected material by chest tube and also by clearing pleural drainage pores thereby re-establishing pleural circulation.

In a landmark study, Thomson et al conducted a randomised controlled study in 60 children comparing 6 doses of urokinase against normal saline in the UK [52]. Results suggested that intrapleural urokinase significantly reduced hospital stay by 2 days, although 5 patients (2 in the treatment arm) failed treatment and required surgical decortication. On further analysis, for a sub-set of children with small pigtail drains hospital stay was further reduced. Seven paediatric case series involving 136 patients treated with fibrinolytics have been published and these have demonstrated a successful outcome without the need for further surgical intervention in 111 of 123 cases (90%).

Open thoracotomy is not recommended as a treatment of childhood empyema as it has largely been superseded by the use of VATS. There are no randomised studies of childhood empyema treated with open thoracotomy and it is actively discouraged due to the morbidity associated with a scar. The use of VATS as a primary treatment for empyema has grown in recent years [64]. The advantages over open surgery are that it is minimally invasive and the small scars limit tissue damage. Furthermore, it offers the advantage of better visualisation of internal structures compared to open surgery. The clinical outcomes are better with VATS when compared to those children treated with chest drain alone [63]. However, the disadvantages are that the equipment is expensive and requires surgical expertise which may not be available in all centres, particularly non-tertiary hospitals.

In a randomised controlled study in London, UK, the use of urokinase through a soft small bore percutaneous drain was compared with VATS in 60 children [25]. This study concluded that there was no significant difference in length of stay after intervention, total length of stay, or radiologic outcomes 6 months after intervention between the 2 treatment arms [25]. This study was replicated using alteplase in the USA with virtually identical results [26]. Importantly both studies demonstrated that VATS was significantly more expensive. This was further supported by cost analysis of the different strategies for the treatment of paediatric empyema which showed that treatment with fibrinolytics is the cheapest option [65]. One USA study, specifically designed to compare costs of VATS and chest tube placement demonstrated no difference in financial burden [24]. However, they excluded children less than 12 months as they believed that VATS was technically difficult and less likely to be performed in this age group. More importantly, the children with primary chest drain did not have fibrinolytics instilled.

Thus we recommend the use of small bore (size 8-12 F) percutaneous drains together with the instillation of fibrinolytics or the use of VATS as the optimal intervention of choice in children with empyema. The decision depends on local expertise, financial resources and the availability of staff to place a drain. Percutaneous drains inserted using the Seldinger technique are relatively easy to insert compared with the blunt dissection approach using a stiff larger bore drain. They are less invasive and painful and thus encourage mobilisation and coughing which may aid recovery. The concerns that they may block seem to be unfounded if regularly instilled with fibrinolytics. Furthermore, the complexity of the stage of the empyema does not impact on treatment outcome [25].

Evidence from a study in adult patients with empyema suggested that smaller drains inserted using a guidewire were associated with less pain than those inserted by blunt dissection with no adverse affect on outcome [66]. This study needs to be replicated in children.

Each hospital needs to address the easiest pathway for chest drain insertion. This includes whether to use general anaesthesia or sedation and identification of who will place the drain. Ideally this would be done by an interventional radiologist using ultrasound guidance but alternatives include the paediatric, intensive care or surgical staff.

Although there is evidence to support the use of both urokinase and alteplase as fibrinolytics, there is more clinical experience with urokinase in Australia. We therefore recommend the following regimen [25;51;52]. Urokinase should be given twice daily for 3 days (6 doses total) using 40 000 IU in 40 mLs 0.9 % saline for children weighing 10 Kg or more. In those children under 10 Kg, 10 000 units in 10 mLs 0.9% saline should be used. Following each instillation, the chest tube is clamped for 4 hours and the child encouraged to mobilise. After removal of clamp, the chest drain is placed on negative suction pressure of 10-20 cms of H<sub>2</sub>O until the next instillation.

Chest drains can be removed if there is less than 1-2 mLs/kg fluid per 24 hours. The presence of the drain in the pleural cavity itself causes irritation and increased production of pleural fluid and therefore it is not advisable to wait until there is no fluid drainage before removing the drain. The clamping of drains prior to removal is not recommended. A chest X ray should be done following removal, and the presence

of some air in the pleural space is not uncommon and is usually reabsorbed in time.

Figure 1 outlines a scheme for the management of children with empyema.

### **Recommendations:**

- The intervention of choice is either percutaneous small bore drainage with either urokinase or alteplase, or video-assisted thorascopic surgery.  
[STRONG Recommendation, MODERATE QUALITY Evidence]
- Chest drainage alone with a large bore drain alone is not recommended.  
[STRONG Recommendation, MODERATE QUALITY Evidence]
- A chest X-ray should be done following drain removal. [STRONG Recommendation, NO Evidence]

### **TREATMENT FAILURE AND COMPLICATIONS**

Persistent fever is the commonest indication of possible treatment failure, caused by either incorrect antibiotic choice or failure of the antibiotics to penetrate the infected lung tissue or cavity. However, it is recognised that in some cases fever will persist for many days due to lung necrosis and inflammation rather than continued sepsis. The pattern of fever should be observed and if this is generally improving then persistence with the chosen treatment regimen should continue rather than changing antibiotics or organising further interventions however tempting. Additionally in these circumstances, a decrease in white blood cells and C-reactive protein is reassuring. A CT scan is indicated for persistent fever which is not reducing and a rise in WBC and C-reactive protein, to exclude a pulmonary abscess or other collection of pus which may not be visible on a chest X-ray. A persistent lobar collapse is unusual and is an indication for a bronchoscopy to exclude a foreign body. Otherwise, there is no indication for a routine bronchoscopy in children with empyema.

Cavitary necrosis, necrotising pneumonia and pneumatoceles may be present on CT scans and are often a complication of empyema [42]. Necrotising pneumonia may result in a prolonged hospital stay but reassuringly the outcome is still excellent [67].

However, in most instances the finding of these parenchymal abnormalities does not change management and is not an indication for routine CT scans [42].

Another potential complication is a lung abscess. While some physicians advocate percutaneous drainage of the abscess itself [68], the potential risk of a bronchopleural fistula means that most physicians recommend treatment with prolonged antibiotics.

A bronchopleural fistula occurs occasionally following the insertion of a chest drain or surgery for the treatment of empyema due to the fragility of lung parenchyma, which leads to a persistent air leak. In these circumstances negative suction on the chest drain is best avoided to improve the chances of tissue healing. Very occasionally surgical intervention is required to repair the fistula.

## **DISCHARGE AND FOLLOW UP**

Once a patient has no oxygen requirement and has been on oral antibiotics for 24 hours then he/she can be discharged. As discussed above, oral antibiotics should be continued for at least one week and may be continued for up to 6 weeks. A follow up chest X-ray should be done at 4 to 6 weeks to ensure that resolution is occurring. This X-ray will not be normal in most instances despite complete clinical recovery of the child and should not alarm the paediatrician as radiological recovery lags behind clinical recovery and in nearly all circumstances some residual thickening is present even as late as 6 months after discharge [25]. There is no need for further imaging unless there is persistent lobar collapse or there are ongoing clinical symptoms. Furthermore, there is no need for further investigations for the cause of empyema in previously healthy children without a history of recurrent infections.

**Recommendations:**

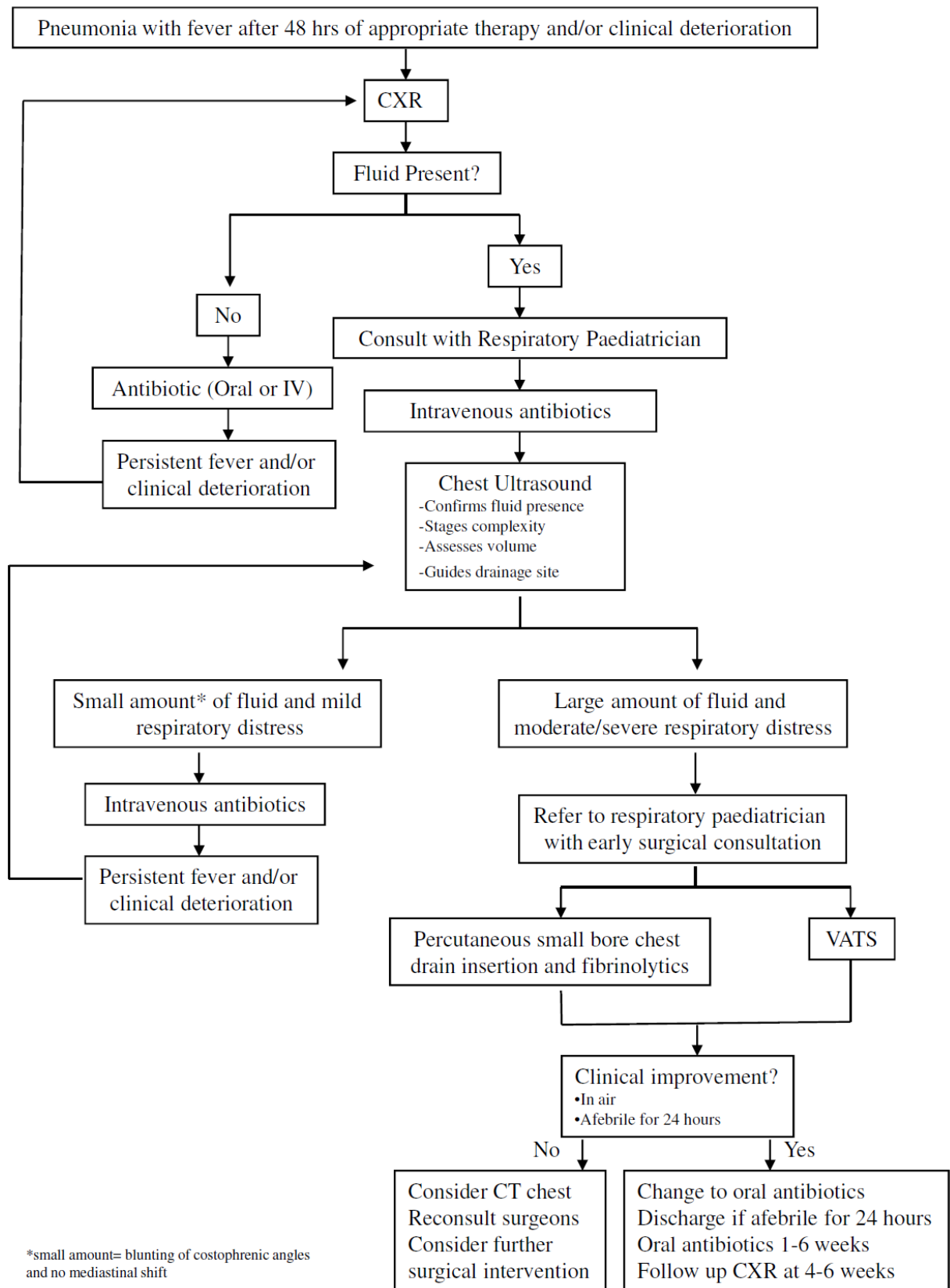
- Children can be discharged if in air and afebrile for 24 hours on oral antibiotics. [WEAK Recommendation, MODERATE QUALITY Evidence]
- A repeat chest X-ray should be done at 4 to 6 weeks post discharge to confirm changes are resolving; most CXR are not completely normal at this time point. [WEAK Recommendation, NO Evidence]
- There is no need for further imaging unless there are persistent clinical symptoms or complications. [WEAK Recommendation, NO Evidence]
- There is no need for further investigations to identify a possible underlying cause in previously healthy children without a history of recurrent infections. [WEAK Recommendation, VERY LOW QUALITY Evidence]

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**Figure 1**

Pathway for the management of children with empyema



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