

LRI Children's Hospital

Pleural empyema and necrotising pneumonia in children

Staff relevant to:	Medical & nursing staff caring for Children admitted to UHL Children's Hospital with para-pneumonic effusions and empyema.
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The original version of this guideline was based on the recommendations issued by the BTS in 2005 ⁽¹⁾. Considering that the original BTS recommendation is now dated, this revision takes into account other evidence, and evidence based guidance issued by other authorities ^(2, 3).

Contents

Related documents:.....	2
1. Introduction and Who Guideline applies to.....	2
2. PART 1 – Parapneumonic effusions and empyema.....	3
a) Aetiology	3
b) Investigations and management.....	3
Figure 1: Algorithm for the management of parapneumonic effusions in children ..	4
c) Acute management:.....	5
d) Investigations:.....	5
e) Management:.....	5
a. Antibiotic therapy:.....	5
Table 1: Antibiotic management of empyema.....	6
f) Surgical management:.....	7

g) Urokinase therapy	7
h) Discharge and follow-up:	8
3. PART 2 – Necrotising pneumonia	9
a) Aetiology:.....	9
b) Investigations and management:.....	9
c) Antibiotic therapy	9
Table 2: Antibiotic management of necrotising pneumonia	10
d) Surgical intervention	11
e) Discharge and follow-up:.....	12
4. Education and Training	12
5. Monitoring Compliance.....	12
6. Supporting References.....	13
7. Key Words.....	14
Appendix 1: Procedure for Administering Intrapleural Urokinase	15
Intrapleural urokinase is an effective intervention in the management of paediatric empyema. ⁽¹¹⁾	15

Related documents:

UHL ref C41/ 2016 - [Chest drain insertion and management UHL Children's Hospital & Paediatric Intensive Care Guideline](#)
UHL ref C96/2016 - [Pneumonia - Inpatient UHL Childrens Hospital Guideline](#)
UHL ref C8/2019 - [Tuberculosis UHL Childrens Hospital Guideline](#)

1. Introduction and Who Guideline applies to

This guideline is applicable to para-pneumonic effusion, pleural empyema, and necrotising pneumonia (NP) admitted to UHL Children's Hospital. It should be read alongside the community acquired pneumonia guideline and the chest drain in children guideline.

Complicated pneumonia should be suspected in cases of community acquired pneumonia if there is evidence of treatment failure (persisting high fevers, high inflammatory markers). Clinical examination findings (dullness on percussion) and Chest X Ray may suggest associated effusion. Ultrasound chest confirms presence of fluid in pleural space.

This guideline does not apply to the following special situations:

- **Empyema following trauma**

- Iatrogenic empyema (e.g. due to mediastinal or pleural procedures).
- High suspicion of non-infective pathology (e.g. malignancy).

Definitions:

Parapneumonic effusion: A collection of clear inflammatory fluid in pleural cavity (usually neutrophilic exudate) in association with underlying pneumonia.

Empyema: Presence of pus in pleural space. Deposition of fibrin with septations and loculations are characteristic of empyema.

Necrotising pneumonia: A severe form of pneumonia characterised by formation of cavities and abscesses in lung parenchyma, usually associated with significant pleural involvement.

2. PART 1 – Parapneumonic effusions and empyema

a) Aetiology

Commonly isolated organisms in paediatric pleural effusions are *Streptococcus pneumoniae*, *Streptococcus pyogenes* and *Staphylococcus aureus* ^(4,5).

Mycobacterium tuberculosis may be associated with parapneumonic effusions, especially in presence of risk factors (chronic illness, travel history to endemic area, contact history, non-response to standard treatment etc.), be vigilant of M. tuberculosis especially in patients with risk factors. Refer to paediatric TB guidelines. It must be noted that sensitivity of bacterial cultures of pleural fluid is <20% in children ^(5,6) Specialised techniques like broad range 16S rDNA PCR may be required ⁽⁵⁾.

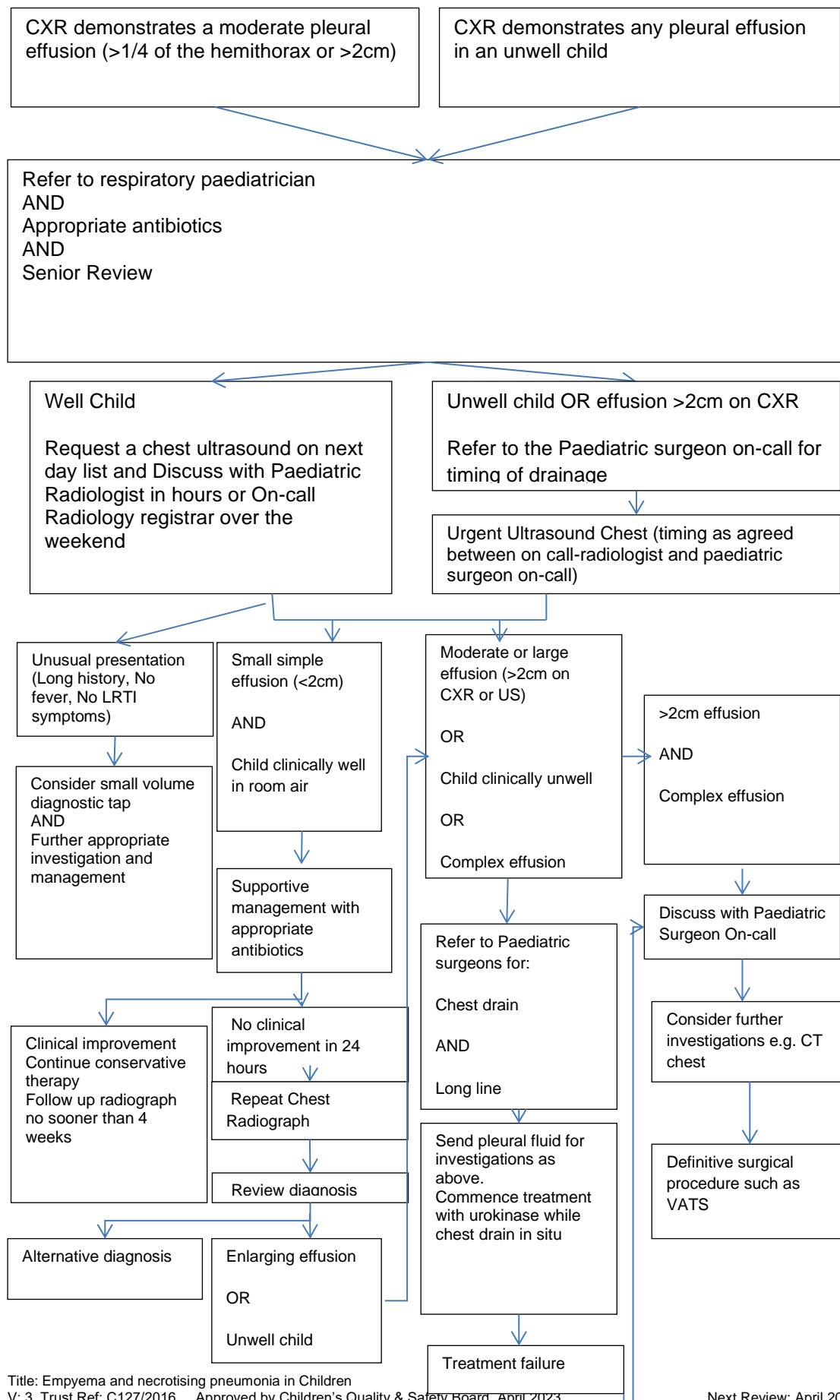
There is evidence that bacterial pathogens may be dissimilar between bacterial pneumonia and bacterial infections of the pleural space ⁽⁷⁾. This may be due to the acidic and hypoxic environment of infected pleural space favouring selected pathogens ⁽⁷⁾. Many anaerobic bacteria infecting pleural space cannot tolerate the high pO₂ of lung parenchyma and may not be easy to detect on cultures.

b) Investigations and management

Please refer to flowchart as per figure 1.

Contact the paediatric respiratory team at the earliest opportunity and let the surgical on-call team know early about the child.

Figure 1: Algorithm for the management of parapneumonic effusions in children



c) Acute management:

- I. Assessment and supportive management: ABC approach to assessment and supportive management, including management of fever, hypoxia and respiratory failure should proceed as per standard practice/APLS guidance.
- II. Specific points: On admission, obtain a detailed history and perform clinical examination. If transferred from another hospital, obtain notes, results of investigations, antibiotic history and imaging from base hospital. If not done in last 24 hours, the child will need a chest radiograph. A senior doctor (registrar and above) should review the chest radiograph and if there is clinical suspicion of an effusion arrange for the chest US.
- III. Radiology: Ultrasound (US) chest is the key investigation for assessing the nature of an empyema. Please liaise with radiology to arrange a time for an US chest.
- IV. Radiology request: examination for suspected pleural effusion. Please assess the presence of fluid and the presence of loculations or echogenic fluid.

d) Investigations:

- Blood tests: FBC, CRP, U&E, LDH, Protein, Glucose, ASOT, EDTA blood for pneumococcal PCR, serum for atypical pneumonia screen including Mycoplasma serology, Blood Culture
- Point of care (POC) testing for respiratory viruses (influenza, RSV and COVID)
- Nasopharyngeal secretions and/or nasal swabs for viral detection and atypical bacterial PCR
- Consider sending a urine sample for pneumococcal antigen testing in children ≥ 10 years old.
- Respiratory secretions/endotracheal aspirate for MC&S. (Note that sputum and tracheal aspirate cultures are typically poor guides for empyema management as they may not reflect the relatively anaerobic milieu of empyema)
- If obtained, pleural fluid analysis is very useful (see page 10)
- 16S PCR (If culture is negative, discuss with microbiologist for consideration of 16S PCR).

e) Management:

The two important parts of management of empyema are antibiotics and chest drains with urokinase instillation.

a. Antibiotic therapy:

Antibiotic management of parapneumonic effusion: This is similar to antibiotic management of community acquired pneumonia (CAP). Please refer to CAP guidelines (see related documents). If there are organisms identified in blood culture, tailor the antibiotic to the organism.

Antibiotic management of empyema: To be used when there is US evidence of pus in pleural space- see table 1.

Table 1: Antibiotic management of empyema

	<u>First Line</u>	<u>Second Line</u>	<u>Special Cases</u>
Acute phase	Co-amoxiclav iv + Clarithromycin [use clarithromycin only if Mycoplasma suspected] Discuss microbiology to consider adding Clindamycin if child has severe sepsis or toxic shock [¥] .	Unable to tolerate first line: cefuroxime +/- metronidazole Non response to first line: consider change of antibiotics after discussion with microbiology consider unusual organisms	Allergy to beta-lactams: Take full history of allergy. Liaise closely with microbiology and pharmacy.
Continuation phase	Oral co-amoxiclav (severe infection dose) is preferred. Discuss with microbiology if previous treatment failure with co-amoxiclav or inability to tolerate oral co-amoxiclav. Treatment is adjusted according to pleural fluid culture/sensitivity results if available.		Discuss with microbiology and pharmacy
Criteria for switch to continuation phase	Switch to oral antibiotics 24 hours after drain removal (or) after criteria* are met in children managed without chest drain. Monitor for at least 24 hours in hospital after switch to oral antibiotics		
Duration of continuation phase	A minimum total antibiotic duration of 28 days, and at least 2 weeks from draining and/or VATS surgery. Arrange post-discharge appointment at end of course to review if further antibiotics required. Also see discharge/follow-up section below.		

* Criteria for switch to oral antibiotics in children without chest drain:

- Afebrile for 24 hours (Note: One off spikes of temperature separated by >24 hours are common during recovery phase). Treatment failure is suspected when > 1 spike per day and temperature > 39 degrees.
- Making good clinical progress (i.e. off respiratory support/ oxygen therapy, PEWS score/ work of breathing improving)
- Inflammatory markers improving.

For Doses, please refer to the current edition of BNF for children.

¥If Toxic Shock Syndrome is suspected, please refer to ([Toxic Shock Syndrome UHL Childrens Guideline](#)) for further management.

f) Surgical management:

Please discuss with both the paediatric respiratory and paediatric surgical teams for a joint decision-making.

Narrow bore chest drains are not usually indicated in empyema < 2 cm depth from pleural surface (usually resolve with antibiotics alone) and loculated posterior empyemas (difficult access).

Generally surgeons would prefer to drain empyemas of a depth of more than 2 cm, in view of safety. The decision to drain or not is not based on the arbitrary number, but is based on the clinical condition and response to treatment. Following the introduction of appropriate antibiotics, the decision to proceed to drainage should take into consideration a number of factors, including the clinical and laboratory response to antibiotic therapy at 48–72 h, or evidence of an enlarging effusion on repeated ultrasound.

Narrow bore chest drain insertion + urokinase has become the mainstay of management of paediatric empyemas ⁽¹⁾. It is equally effective as, less invasive than and less costly than video-assisted thoracoscopic surgery (VATS) and large bore chest drain insertion ^(8,9).

In children with loculated collections, evidence of air leak (necrotising process) or thick debris in pleural fluid, primary VATS procedure may be preferred.

Surgical Team: If a decision is made to drain the effusion, a narrow bore catheter should ideally be inserted in theatre, under GA (see related documents- paediatric chest drain guidance). Urokinase is ideally instilled into the chest immediately following chest drain insertion.

PLEASE insert a long line or similar whilst under anaesthetic as these children tend to need prolonged courses of IV antibiotics.

Pleural fluid analysis

Send pleural fluid for

- Biochemistry (glucose, pH, lactate dehydrogenase(LDH) and protein)
- Cytology (cell count and cell differential)
- Microbiology (Gram stain, acid-fast bacilli stain, culture, and antibiotic sensitivity testing).
- Pneumococcal antigen, and atypical pneumonia PCR testing
- Request 16S PCR if there is no growth on the culture.

g) Urokinase therapy

Intrapleural instillation of urokinase is recommended in all children with paediatric empyema without an ongoing air-leak syndrome.

- Children over 12 months: 40,000 units made up in 40mls of 0.9% sodium chloride 12 hourly
- Children under 12 months: 10,000 units made up in 10mls of 0.9% sodium chloride 12 hourly

Dose and preparation guidance is on Medusa

Usual course: 6 doses in total

Appropriately trained medical and nursing staff can instill Urokinase intrapleurally

For urokinase administration see Appendix 1.

h) Discharge and follow-up:

Removal of chest drain:

Leave chest drain in for 6 doses of urokinase. Further doses of urokinase are rarely required (this is a consultant decision). Normal pleural fluid secretion is 0.3 ml/kg/day. Presence of a foreign body (chest drain) can increase the secretion to 1-2 ml/kg/day.

If 24 hour drain output is less than 1ml/kg/day the drain can be removed (see chest drain guidance).

Switch to oral antibiotics:

Monitor in hospital for 24 hours after the switch to oral antibiotics and consider re-investigation and treatment if clinical or inflammatory parameters worsen (table 1). Note that empyema can never be completely drained, and it is usual to have fever spikes (albeit less frequent and lower temperatures) for a few weeks. This is the main reason for prolonged course of oral antibiotics.

Discharge criteria:

- fever <37.5 for 24 hours
- No respiratory distress
- Saturations maintained in air
- Documentation of reduction of pleural fluid levels.

Follow up:

1. A day-case review should be arranged at the end of continuation phase of oral antibiotics to document clinical improvement and improvement of inflammatory parameters. If signs of partial resolution – continue oral antibiotics further.

(Caution—Chest x-ray may not be back to normal. A chest x-ray can be requested if there is suspicion of a worsening or new pathology like a necrotizing process)

2. The child is booked for a follow-up appointment in the general respiratory clinic in 3 months.

3. PART 2 – Necrotising pneumonia

Necrotising pneumonia (NP) is a rare but severe complication of pneumonia characterized by necrosis, cavity formation or abscess in the pulmonary parenchyma. It is frequently associated with concomitant pleural disease. Because of rarity and variations in presentation, there are no clear evidence based guidelines for NP. In all cases, therefore, it should be managed by a specialist team comprising at least paediatric respiratory and paediatric surgical teams.

a) Aetiology:

Masters et al ⁽¹⁰⁾ identified 9 studies of paediatric necrotizing pneumonia where more than 20 patients were reported. Following organisms were identified based on blood culture or pleural culture: *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Streptococcus pyogenes*, *Fusobacterium* species, *Streptococcus anginosus*, *Pseudomonas* species. It was acknowledged that many case series have not performed anaerobic cultures. Therefore, the incidence of anaerobic bacteria may be underestimated.

b) Investigations and management:

Management of NP is a multi-disciplinary team approach of paediatric respiratory physicians, Intensivist, thoracic surgeons, and microbiology /infectious diseases experts. The aims are to control and ultimately reverse the pathobiology changes associated with NP. Consider secondary infection of an existing undiagnosed congenital lung malformation in the differential diagnosis if radiological changes do not correlate with clinical picture or progress of patient.

- I. Supportive therapy should proceed as per PART 1 empyema section c (i, ii).
- II. Radiology: Chest x ray is not sensitive in diagnosis of necrotizing pneumonia (27-41% sensitivity). Air leak into the pleural cavity, such as pneumothorax in the presence of pneumonia or pyopneumothorax and lucencies in lung parenchyma are signs of NP. US chest is not the recommended modality of investigation, as ultrasound is reflected by air- tissue interface.
- III. The standard radiological investigation in NP is CT chest ⁽¹⁰⁾. Liaise with paediatric surgeons and paediatric respiratory physicians re: timing of CT chest.

c) Antibiotic therapy

Recommendations for initial antibiotic therapy are similar to empyema, and the second-line therapies are shown in table 2.

Table 2: Antibiotic management of necrotising pneumonia

	<u>First Line</u>	<u>Second Line</u>	<u>Special Cases</u>
Acute phase	<ul style="list-style-type: none"> •Co-amoxiclav iv •Discuss with microbiology for consideration of clindamycin if suspecting/isolating Group A Strep, Staph aureus, or toxic shock[¥]. 	<ul style="list-style-type: none"> •Expert guidance from respiratory consultant AND microbiology consultant must be sought. Expert guidance from surgeons on risk vs benefit of surgical intervention must also be considered at this stage. •See considerations for antibiotic cover* 	<u>Allergy to beta-lactams:</u> Take full history of allergy. Liaise closely with microbiology and pharmacy. <u>PVL producing Staph / MRSA NP:</u> Liaise with microbiology and pharmacy, and also consider discussing with Infection prevention/UKHSA regarding decolonisation of household members
Continuation phase	Oral Co-amoxiclav (severe infection dose) Discuss with microbiology if previous treatment failure with co-amoxiclav or inability to tolerate oral co-amoxiclav. Treatment is adjusted according to pleural fluid culture/sensitivity results if available.		Discuss with microbiology and pharmacy
Criteria for switch to continuation phase	Switch to oral antibiotics when criteria** are met. Some children have surgical chest drain +/- VATS surgery. Continue IV antibiotics at least until the drain is removed in these cases. Monitor for at least 24 hours in hospital after switch to oral antibiotics		
Duration of continuation phase	A minimum total antibiotic duration of 28 days ⁽¹⁰⁾ , and at least 2 weeks from draining and/or VATS surgery. Arrange post-discharge appointment at end of course to review if further antibiotics required. Also see discharge/follow-up section below.		

***Considerations for second line IV antibiotics:**

- Consider pleural fluid culture/sensitivity or 16S RNA results, if available
- Consider secondary infection elsewhere (vs. non-resolution of primary infection)
 - E.g. intercurrent viral infection, septic emboli, line infection
- If the child/inflammatory markers are improving but X-Ray picture doesn't improve as expected, consider whether it could be an infection on an existing (previously undetected) congenital airway malformation.
- Consider surgical intervention to drain pus (But see v, below)
- Consider other rare organisms, especially in following context
 - Foreign travel, immunodeficiency, hospital acquired pneumonia.

****Criteria for switch to oral antibiotics in children with NP:**

- Afebrile for 24 hours (Note: One off spikes of temperature separated by >24 hours are common during recovery phase). Treatment failure is suspected when > 1 spike per day and temperature > 39 degrees.
- Making good clinical progress (i.e. off respiratory support/ oxygen therapy, PEWS score/ work of breathing improving)
- Inflammatory markers improving.

Chest drain: Routine insertion of urokinase therapy is not recommended, especially in the presence of pneumothorax.

Surgical management: In the absence of concomitant pleural disease (E.g. many cases of isolated lung abscess), antibiotic therapy alone may be adequate⁽³⁾. Caution is needed before embarking on surgical intervention ⁽³⁾, because of the risks of bronchopleural fistula and uncontrollable bleeding.

Close liaison is recommended between the paediatric surgical team and paediatric respiratory team.

¥ If Toxic Shock Syndrome is suspected, please refer to **Toxic Shock Syndrome UHL Childrens Guideline** for further management

d) Surgical intervention

There are 2 main goals of surgical intervention:

1. Manage concomitant pleural disease: VATS procedure and chest drain is preferred – liaise with paediatric surgeon.
2. Management of progressive parenchymal necrosis. Surgical intervention may be required to relieve mass effect (tension pneumatocele) or massive hemoptysis. Segmental resection, Lobar resection or even pneumonectomy may be required ⁽¹⁰⁾.

Duration of hospitalisation can be prolonged due to complications such as bronchopulmonary fistulas and lung abscess.

e) Discharge and follow-up:

Discharge criteria:

- Fever <37.5 for 24 hours after conversion to oral antibiotics
- No respiratory distress
- Saturations maintained in air
- Absence of evidence of persisting air leak or increasing fluid collection in pleural space.

Follow up:

Most of the children make good recovery with a near normal CXR by 3 months.

1. A day-case review should be arranged at the end of course of oral antibiotics to document clinical improvement and improvement of inflammatory parameters. If signs of partial resolution – continue oral antibiotics further.

(Caution - Chest X-ray may not be back to normal. A chest x-ray can be requested if there is suspicion of a worsening or new pathology).

2. The child is booked for a follow-up appointment in the general respiratory clinic in 3 months.

4. Education and Training

Ongoing education for medical staff through departmental meetings.

5. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Recommended investigations are done in children with empyema (blood tests, USS chest and recommended pleural fluid tests)	Audit	M. Ramphul	3 yearly	Local clinical audit/practice group
All empyemas without evidence of air leak should	Audit	M. Ramphul	3 yearly	

have recommended duration of urokinase therapy		M. Ramphul		
Recommended antibiotic therapy is given. In case of deviation, the reason for deviation is documented in notes	Audit		3 yearly	
Day case review is arranged for all children with empyema following discharge to document improvement before antibiotics are stopped	Audit	M. Ramphul	3 yearly	

6. Supporting References

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Children with Pleural Empyema: A Randomized Clinical Trial. JAMA Pediatr. 2020 Apr 1;174(4):332-340.

7. Key Words

Chest drains, Empyema, Necrotising pneumonia (NP), Para-pneumonic effusions, Respiratory, Urokinase

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs. As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

CONTACT AND REVIEW DETAILS	
Guideline Lead (Name and Title) Manisha Ramphul, Paediatric Respiratory Consultant	Executive Lead Chief Medical Officer
Details of Changes made during review: Radiology section updated Change in the depth of the empyema amenable to drainage Microbiology investigations updated Advice on urokinase explained and appendix added Discharge plans and follow-up arrangements included	

Appendix 1: Procedure for Administering Intrapleural Urokinase

Intrapleural urokinase is an effective intervention in the management of paediatric empyema.⁽¹¹⁾

1. Inform the Nurse in Charge that procedure is required. Determine if it is appropriate for nursing staff to administer. If not, escalate to the medical team to administer. In the event that the drain does not have a 3 way tap – submit an incident report (Datix).
2. Inform the patient and/or family of procedure. Obtain informed consent.
3. Check local guidance for preparation of Urokinase and prepare using ANTT principles using IV drug tray (following IV policy as per Medusa - Paediatric Injectable Medicines Guide).
4. Wear appropriate PPE and adhere to 5 moments of hand hygiene.
5. Maintain privacy and dignity. Maintain a safe area ensuring emergency equipment is available including two clamps and a sterile dressing. Maintain a clean environment i.e. turn off fans.
6. Ensure patient is on continuous oxygen saturation monitoring throughout administration of Urokinase.
7. It is recommended that a sterile towel is placed between the patient and drain.
8. Close 3 way tap to patient (Figure 2) Attach a clamp to the drainage tubing near the 3 way tap. Avoid clamping the chest drain itself as it predisposes a risk of accidental displacement due to weight of the clamps.
9. Remove bung and discard. Clean access port on drain using Chlorhexidine 2% and Alcohol 70% wipe, firstly scrub the top of the port for at least 10-15 seconds and then using an alternative place on the wipe scrub the sides of the access port for 10-15 seconds and leave to dry for 30 seconds.
10. Attach luer lock syringe containing Urokinase to access port on the 3 way tap.
11. Close 3 way tap to drainage bottle and open up to patient (Figure 3).

12. Instil Urokinase gently into the pleural cavity over 5 minutes or longer depending on patient's tolerance. Monitor throughout for any changes in clinical condition. If concerned, stop procedure and escalate.
13. On completion, close 3 way tap to the patient (Figure 4).
14. Disconnect syringe. Clean access port using Chlorhexidine 2% and Alcohol 70% wipe, firstly scrub the top of the port for at least 10-15 seconds and then using an alternative place on the wipe scrub the sides of the access port for 10-15 seconds and leave to dry for 30 seconds. Apply a clean bung.
15. Leave 3-way tap closed and clamps in-situ for 4 hours.
16. Drain insertion site, 3 way tap and clamps must be checked hourly. Additional hourly checks of the volume in the drainage bottle must also be monitored to ensure that no further drainage occurs.
17. Vital signs must be monitored as per the Children's Hospital Chest Drain Management Policy ([include link to policy here](#))
18. After 4 hours remove clamps and open 3 way tap to allow drainage (Figure 5).
19. In the absence of a 3-way tap, the drain and drainage tube are clamped, and disconnected. A bladder syringe is then used to instill urokinase to the chest drain. The drain and drainage tube are then connected, but left clamped for 4 hours
20. Document using Chest Drain Monitoring sheet and patient's medical notes.

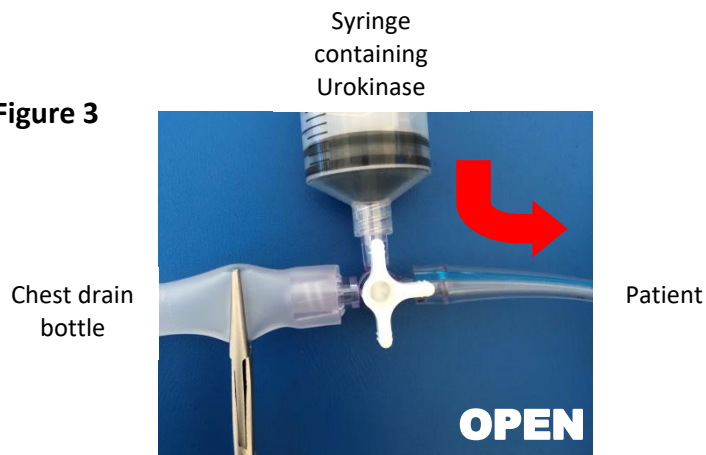
Correct use of the 3 way tap

Figure 2



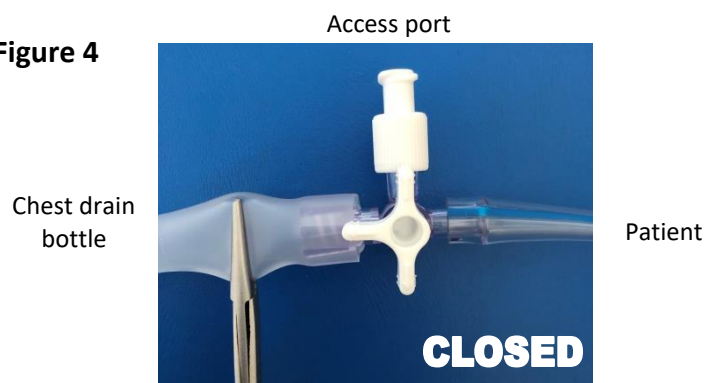
Clamp drainage tubing, make sure 3-way tap is in this position whilst cleaning the access port and then attach the syringe containing Urokinase.

Figure 3



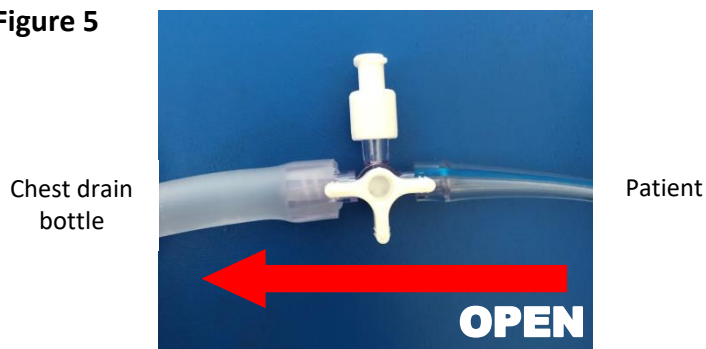
Once syringe containing Urokinase is attached to the access port, turn 3-way tap to this position, to open to the patient.

Figure 4



Whilst Urokinase is insitu for 4 hours, return the 3-way tap to this position and apply a clean bung. Check drain hourly to make sure it is still in correct position.

Figure 5



After 4 hours, remove the clamp and put the 3-way tap in this position to allow the fluid to drain into the drainage bottle, it also prevents any potential leak from the access port.