SESLHD PROCEDURE COVER SHEET

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AUTHOR	A/Prof Ben Kwan Sutherland Hospital Director Respiratory Medicine
POSITION RESPONSIBLE FOR THE DOCUMENT	Cardiac Respiratory Stream Director / Manager Suzanne.schact@health.nsw.gov.au
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KEY TERMS	Empyema, Intra-pleural Fibrinolysis, Alteplase / Dornase Alfa, intra-pleural fibrinolytic therapy, Respiratory
SUMMARY	Intra-pleural Fibrinolysis, in appropriately selected patients, is an option for the treatment of empyema or fibrin bands that develop within complex pleural fluid collections. Intra-pleural fibrinolysis is aimed at dissolving the fibrin bands that develop within a complex pleural fluid collection or empyema and will aid the drainage of that effusion / collection. This is performed via an intercostal catheter or pigtail pleural catheter, inserted into the pleural space to remove fluid from the pleural cavity and attached to an underwater seal drain (UWSD). Current evidence recommends, instillation of a solution of 5mg dornase alfa in 50mL of sodium chloride 0.9% and 5mg alteplase in 50mL of sodium chloride 0.9% into the pleural cavity every 12 hours up to three consecutive days.

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Intra-Pleural Fibrinolysis – Medical Management of Empyema

SESLHDPR/631

1. POLICY STATEMENT

This procedure should be used in conjunction with:
NSW Ministry of Health Information Bulletin IB2020_010 - Consent to Medical and Healthcare Treatment Manual
NSW Ministry of Health Policy Directive PD2017_032 - Clinical Procedure Safety
NSW Ministry of Health Policy Directive PD2013_043 - Medication Handling in NSW Public Health Facilities
SESLHDPR/528 - Procedural Sedation (Adults, Ward, Clinic and Imaging areas)
SGSHHS Underwater Seal Drain (UWSD)
SGSHHS Intravenous (IV) medication, therapy and additives
NSW ACI ACI/D14/2115 Minimum Standards - Safe Procedural Sedation
NSW ACI ACI/D14/1571 Pleural Drains in Adults A Consensus Guideline.

2. BACKGROUND

Treatment Aim:

- Intra-pleural Fibrinolysis, in appropriately selected patients, is an option for the treatment of empyema or fibrin bands that develop within complex pleural fluid collections. Other therapeutic alternatives include surgical decortication or video-assisted thoracoscopic (VATS) procedure (i.e. performed by a cardiothoracic surgeon in an operating theatre). Intra-pleural fibrinolysis can be used where other therapeutic alternatives are inappropriate or contra-indicated.
- Intra-pleural fibrinolysis is aimed at dissolving the fibrin bands that develop within a complex pleural fluid collection or empyema and will aid the drainage of the effusion / collection. Treatment includes instillation of a solution of 5mg dornase alfa in 50mL of sodium chloride 0.9% and 5mg or 10mg alteplase in 50mL of sodium chloride 0.9% into the pleural cavity via an intercostal catheter or pigtail pleural catheter connected to an UWSD.*
- Suction to aid pleural drainage before and after Intra-pleural fibrinolysis is usually unnecessary. When suction is applied it should be low wall suction not exceeding 5kpa.
- This procedure may be performed twice daily up to three consecutive days (total 6 doses, with at least 6 hours in between doses).

Definitions and Abbreviations:

Empyema	A collection of purulent material in the pleural space. Usually secondary to pneumonia.
Intercostal catheter (ICC)	A catheter enabling drainage of air or fluid from the pleural space, allowing negative intra-thoracic pressures to be re-established leading to lung re-expansion.
Loculations/septations	A group of chambers / cavities usually isolated from surrounding structures (as by a fibrous tissue septum).
Pigtail pleural catheters (PPC)	A small bore catheter specifically used in draining loculated pleural effusion. PPC are efficacious and comfortable with minimal risk of complications.
Tunnelled indwelling pleural catheter (TPC)	Soft silicone small bore catheter surgically inserted, that allows intermittent ambulatory drainage of pleural fluid into underwater seal drainage system or plastic vacuum bottles.
Pleural effusion	A collection of fluid in the pleural space. The fluid restricts expansion of

	the lung reducing vital capacity and the volume of air available for gas exchange.
Video-assisted thoracoscopic surgery (*VATS)*	Video-assisted thoracoscopic surgery is a type of thoracic surgery performed using a small video camera that is introduced into the patient's chest via small incisions.

Indications for intra-pleural fibrinolysis

- Community or hospital acquired pneumonia complicated by thoracic empyema or pleural sepsis as defined by pleural fluid with the physical characteristics of pus, a positive gram stain for bacteria, pH<7.10, lactate dehydrogenase (LDH) >1000IU/L, pleural fluid / blood glucose ratio <0.25 and differential cell count confirming a predominance of neutrophils (>10000/mm^3 or $10x10^9$/L)
- Loculations / septations may be confirmed on ultrasound (preferable) or CT scan imaging.

Contraindications for Fibrinolytic

1. Treatment with streptokinase (not available in Australia), dornase alfa or urokinase in the past two years for empyema (excluded in MIST-2). Repeated systemic administration of streptokinase has been linked with a higher incidence of allergic reaction and formation of anti-streptokinase antibody which may reduce its therapeutic efficacy
2. Past medical history of coagulopathy, excessive bleeding states or anticoagulation / antiplatelet medications **(recommend INR < 4 and partial thromboplastin time (PT) < 50s)**
3. Presence of a bronchopleural fistula
4. Haemorrhagic stroke, cranial neoplasms, cranial surgery, head trauma within the preceding 14 days or recent major surgery within 10 days. **Discussion with the Neurologist involved or Surgeon (if patient has had recent surgery) is advised**
5. Previous hypersensitivity reaction to dornase alfa or urokinase / streptokinase
6. Overwhelming sepsis.

Patients on antiplatelet agents or anticoagulants

- In patients on antiplatelet agents (other than aspirin) or therapeutic anticoagulation, the medication should be withheld before administration of intrapleural fibrinolytics if it is clinically feasible and appropriate. Discussion with relevant AMO or Haematology regarding clinical need of antiplatelet/anticoagulants is advised
- In patients with clinically significant systemic coagulopathy, fibrinolytics should be avoided unless the coagulopathy is corrected.

Prerequisites for Fibrinolytic

- Patients selected for fibrinolytic therapy should have clear clinical and laboratory evidence of a complex pleural effusion or empyema
- There should be evidence of lung re-expansion without evidence of bronchial obstruction or fibrotic-trapped lung after the pleural effusion has been drained.

Lower dosing

- There is clinical report to suggest that starting with dosage less than 5 mg alteplase might be as effective as 5mg alteplase, and emerging evidence 5mg alteplase is as effective as 10mg alteplase. If lesser dosage of alteplase is administered, dose escalation up to 10 mg may be considered if clinical and radiological improvement is not seen
- There is weak evidence to suggest that once or twice daily instillation of intrapleural alteplase and dornase alfa have similar efficacy and safety. If a once daily regimen is selected, changing to twice daily dosing should be considered if clinical and radiological improvement is not seen.

3. RESPONSIBILITIES

3.1 Line Managers will: ensure staff have the necessary training to perform their clinical roles in relation to this procedure and have access to necessary equipment. That a dedicated airway monitor is present throughout the procedure if sedation is given.

3.2 Medical staff will: undergo any necessary training in relation to performing the procedure. The proceduralist will ensure there is a dedicated airway monitor present throughout the procedure if sedation is given.

4. PROCEDURE

4.1 Necessary Equipment / Consumables and Medication / Solutions

Equipment / Consumables	Medications / Solutions
• Large dressing pack and extra wool swabs • 1 x sterile pot / container • 4 x 50ml catheter tip or luer lock syringe • 10 ml syringe • 18g needles • 2 x Howard Kelly (atraumatic/smooth) tubing clamps • Disposable draw sheet • Personal protective equipment including eye protection and sterile gloves • Underwater Seal Drainage system (UWSD) • Sterile labels and pen.	• 5mg of dornase alfa (obtained from pharmacy) diluted in 50mL sodium chloride 0.9% • 5 or 10mg of alteplase (obtained from pharmacy) diluted in 50mL of sodium chloride 0.9% • Sterile bottle 0.9% sodium chloride • Chlorhexidine or iodine antiseptic (ensure no allergy to these agents).

4.2 Pre-procedure preparation

1. An ultrasound of the pleural space must be obtained prior to the procedure to estimate the quantity of fluid, degree of loculation / adhesion within the fluid and incomplete lung re-expansion ("trapped lung").

2. Informed and written consent MUST be obtained as per NSW Ministry of Health Information Bulletin IB2020_010 - Consent to Medical and Healthcare Treatment Manual
3. *Clinical procedure safety checklist Level 3* MUST be conducted to determine correct patient, procedure and site as per NSW Ministry of Health Policy Directive PD2017_032 - Clinical Procedure Safety
4. All patients should be commenced on pulse oximetry prior to and monitored throughout the procedure. A full set of observations including pulse and blood pressure should be undertaken just prior to the procedure according to SESLHDPR/528 – Procedural Sedation (Adults, Ward, Clinic and Imaging Areas)
5. A pleural catheter must be inserted at least 24 hours prior to procedure to allow and assess the amount of pleural fluid drainage.

NB Intrapleural fibrinolysis via TPC is restricted to Sutherland Hospital within SESLHD

4.3 Premedication

- Premedication administered as per written order (for IV medication administration refer to relevant site documents) – if IV midazolam or fentanyl is administered it must be administered by a MO (not the proceduralist) according to NSW ACI ACI/D14/2115 *Minimum Standards - Safe Procedural Sedation*. Flumazenil and naloxone (reversal agent for midazolam and fentanyl respectively) should be readily accessible in the procedural room at the time of the procedure. **NB:** An extra RN for airway management must also be present in compliance with NSW ACI policy
- All medications i.e. alteplase, dornase alfa and sodium chloride 0.9% flushes, premedications must be prescribed on the inpatient medication chart
- Ensure that the patient receives adequate analgesia by using a suitable pain scale to assess the efficacy of analgesia pre and post administration
- If the patient is very anxious, an anti-anxiolytic agent may be considered (co-administration of anxiolytic agent increases the risk of central nervous system depression with midazolam / fentanyl).

4.4 Procedure for Alteplase / Dornase Alfa instillation

Policy Points:

Preparation and instillation of alteplase into the pleural space must be carried out by a MO using aseptic technique.

This procedure may be performed twice daily up to three consecutive days (6 doses). Ensure there is at least 6 hours in between doses.

Number of doses should be individualised on the basis of condition (eg, trends in serum inflammatory markers, fever curve, and white cell count) and radiographic (eg, effusion improvement on chest radiography and bedside ultrasonography) response to treatment

This is a two person procedure. Assistance from a RN is required.

Chest tube should be clamped for at least 1 h after administration of intrapleural fibrinolytic and dornase alfa therapy

A dedicated airway monitor must be present throughout the procedure if procedural sedation is given.

A chest xray post procedure must be ordered, and should be performed within 4 hours.

Suction to aid pleural drainage before and after intra-pleural fibrinolysis is usually unnecessary. When suction is applied it should be low wall suction not exceeding 5kpa.

intrapleural fibrinolysis via TPC is only restricted to Sutherland Hospital within SESLHD

4.4.1 Alteplase / Dornase Alfa Preparation

Step 1. Draw up 10mL of water for injection and inject into alteplase vial to reconstitute it. The solution must be clear and colourless.
Step 2. Add the alteplase solution to the sterile pot container from the large sterile dressing pack.
Step 3. Then add 40mL of sodium chloride 0.9% to the alteplase in the pot. Stir with end of syringe to combine.
Step 4. Draw up the alteplase solution into one 50mL syringe (LABEL it alteplase).
Step 5. Draw up two 2.5mL dornase alfa ampoules and add these to a new sterile pot container.
Step 6. Then add 45mL of sodium chloride 0.9% to the dornase alfa in the pot. Stir with end of syringe to combine.
Step 7. Draw up the dornase alfa solution into one 50mL syringe (LABEL it dornase alfa).

4.4.2 Ensuring Tube Patency

Step 1. Turn off the three way tap or clamped the catheter to the patient.
Step 2. Take a 50mL syringe with 30mL of sodium chloride 0.9% in it.
Step 3. Connect the syringe to either the catheter or three-way tap.
Step 4. Either release the clamp or turn the three way tap towards the underwater sealed drain.
Step 5. Using the 50mL syringe filled with 30mL of sodium chloride 0.9% draw back and insert the sodium chloride 0.9% and then draw back to check patency of the catheter.
Step 6. Unless the catheter fluid is oscillating with respiration then the procedure cannot proceed.

4.4.3 Alteplase / Dornase Instillation

Step 1. Turn the three way tap off or clamp the drain to the patient.
Step 2. Connect the syringe containing alteplase solution to the catheter and release the clamp or three way tap.
Step 3. Slowly inject the solution.
Step 4. Turn the three way tap or clamp the drain to the patient.
Step 5. Attach syringe containing 10mL of sodium chloride 0.9% to catheter.
Step 6. Turn three way tap on and flush the drain.
Step 7. Turn the three way tap off or clamp the drain to the patient for 45 minutes.
Step 8. Unclamp or turn the three way tap on and drain for a further 45 minutes.

Step 9. Connect the syringe containing the dornase alfa solution to the drain and release the clamp or three way tap.
Step 10. Slowly inject the solution.
Step 11. Turn the three way tap or clamp the drain to the patient.
Step 12. Attach syringe containing 10mL of n/sodium chloride 0.9% to catheter.
Step 13. Turn three way tap on and flush the drain.
Step 14. Turn the three way tap off or clamp the drain to the patient for 45 minutes.

4.4.4 Management Post Intra-Pleural Fibrinolysis

- Following instillation of the alteplase / dornase alfa, chest tube should be clamped for at least 1 hour
- The PPC, TPC# or ICC is then allowed to be on free drainage
- Output via the drain may be blood stained. Periodic monitoring of Hb levels is recommended according to the clinical situation
- Post procedure chest X Ray to be performed within 24 hours
- After the alteplase / dornase alfa has been instilled, flush the drain with 20mL of sodium chloride 0.9% every six (6) hours until drain is removed. Sodium chloride 0.9% flushes should be documented in the clinical notes and medication chart
- The number of doses should be individualised on the basis of clinical response (e.g., trends in serum inflammatory markers, fever curve, and white cell count) and radiographic (e.g., effusion improvement on chest radiography and bedside ultrasonography) response to treatment
- Provided the pleural fluid has been drained to the satisfaction of the MO, then the ICC or PPC will be requested for removal as per written medical orders found within the clinical notes
- During the administration of this therapy, vital signs observations are to be attended every 15 minutes, then hourly for 4 hours post therapy
- Required observations as per facility UWSD management CBR (refer to facility UWSD clinical business rule).
    - POWH:
      POWH CLIN003 Chest Drains: Insertion, Management and Removal
    - SGH:
      SGH CLIN 654 Indwelling Pleural Catheter (IPC) Insertion and Monitoring
    - TSH:
      TSH CLIN 620 Insertion Of Intercostal (ICC), Pleural Catheters (PPC), Management Of Underwater Seal Drain (UWSD) And Removal

- The patient should be assessed for pain and receive regular analgesia post procedure as clinically indicated and as prescribed by the MO.

5. DOCUMENTATION

- UWSD chart
- Premedication must be prescribed on the medication chart
- Alteplase / dornase alfa / sodium chloride 0.9% flushes must be prescribed on the inpatient medication chart

- MO to document the procedure, outcome and further instructions in the clinical notes.
- MO to order CXR post procedure
- Nursing staff to document UWSD observations and any unexpected post procedures observations and patient reports of pain post procedure.

6. AUDIT

N/A

7. REFERENCES

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POWH Clinical Business Rule CLIN003 Chest Drains: Insertion, Management and Removal
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TSH Clinical Business Rule CLIN 620 Insertion Of Intercostal (ICC), Pleural Catheters (PPC), Management Of Underwater Seal Drain (UWSD) And Removal

8. REVISION AND APPROVAL HISTORY

Date	Revision No.	Author and Approval
August 2018	DRAFT	Draft approved by Dr Ben Kwan (Author) and Dr Mark Sader (Executive Sponsor)
September 2018	DRAFT	Processed by Executive Services prior to submission to SESLHD Quality Use of Medicine Committee and SESLHD Clinical and Quality Council
October 2018	1	Approved by SESLHD Quality Use of Medicines Committee and SESLHD Clinical and Quality Council for publishing.

October 2021	2	Minor review by A/Prof Ben Kwan (Author). Approved by Executive Sponsor. To be tabled at Quality Use of Medicines Committee.
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