

**Guideline for Anticoagulation & Thrombolysis**

**Incidence:** 18% of children with CVL in place for >48 hours develop venous TE and more than 1.2% of all PICU patients develop arterial catheter related TE in PICU<sup>1</sup>.

**Indication for treatment:** No evidence based recommendation. Clinically important venous thrombosis (suspicion of PE, proximal or central venous thrombus, totally occlusive thrombus, limb or organ threatening thrombus) should be treated<sup>2</sup>. Asymptomatic CVL related thrombosis diagnosed radiologically should also be considered for treatment for risk of pulmonary embolism. Arterial thrombosis is often limb, organ or life threatening or the artery requires to be kept patent and so requires treatment.

**Investigations:** Doppler ultra-sonography for confirmation of diagnosis; Venography is gold standard for diagnosis; Trans-thoracic and trans-oesophageal echocardiography, Ventilation-Perfusion scan, CT-angiography of lung, CT or MRI scan of brain as clinically indicated.

**Management<sup>3</sup>**

Inform PICU consultant immediately; Haematologist should be involved as early as possible

**Temporary CVL related Venous thromboembolism**

- Remove CVL if possible; Always remove UVC.  
CVL may be left in situ if CVL is required, its patent and alternative venous access is not available.
- Do not use thrombolytic therapy routinely; consider thrombolysis if life, limb or organ survival is threatened.
- Obtain Doppler ultrasound
- Exclude contraindication to anticoagulation e.g. recent surgery, new cerebral infarct etc
- Commence on IV **Heparin** if there is concern for bleeding or potential for development of coagulopathy; change to LMWH (Low molecular Heparin) in 5-days or when appropriate.

Or

commence LMWH from the start

- **Heparin dosing and adjustments**

*Loading dose:* 75 U/kg iv injection over 10 minutes

*Initial maintenance dose:* Infants <1yr : 28 U/kg/hr  
Children >1yr : 20 U/kg/hr.

*Monitoring :* APTT ratio; Target 2.0-2.5

*Adjustment:*

APTT ratio	Bolus (u / kg) Or Hold	Rate Change	Repeat APTT
<1.7	Bolus 50	+10%	4h
1.7-1.9	-	+10%	6 -12 h or next day (as clinically indicated)
2-2.7	-	-	Next day
2.8-3.2	-	-10%	6 -12 h
3.3-4	Hold 30 mins	-10%	4h
>4	Hold 60 mins	-15%	4h

- **LMWH (Dalteparin) dosing and adjustments**

*Dosage:* (mg/kg/dose), subcutaneous

Neonates - 12 years : 100 units/kg 12 hourly;

12-18 years : 200 units /kg 24 hourly

*Monitoring:* anti-FXa level

Target 0.5-1.0 U/ml 4-6 hrs post-injection

*Adjustment:*

Anti Xa level (U/ml)	Dose Change	Next Anti Xa level
<0.35	↑ 25%	Next day
0.35-0.49	↑ 10%	Next day
0.5-1.0	-	Next week
1.1-1.5	↓ 20%	Next day
1.6-2.0	delay dose 3 h ; ↓ 30%	Next day
>2.0	redose only when anti Xa <0.5 U/ml ; ↓ 40%	Before each dose until anti Xa 0.5 U/ml

Dose reduction may be required in severe renal and hepatic impairment with close monitoring of anti Xa level.

- Continue Dalteparin at therapeutic dosage for 6 -12 weeks
- Arrange ultrasound and haematology follow up in 6 – 12 weeks

**Central Venous Access Device (CVAD) related venous thromboembolism**

- CVADs associated with confirmed thrombosis should be removed after 3-5 days of therapeutic anticoagulation
- If line removal is not possible : supportive care with radiologic monitoring for extension of thrombus; in previously untreated patients, start anticoagulation if extension occurs.
- Anticoagulation with LMWH or Heparin, followed by LMWH between 6 weeks-3 months.
- If CVAD is still in place on completion of therapeutic anticoagulation, a prophylactic dose of anticoagulation should be given till removal of CVAD
- Thrombolytic therapy should not be used unless survival of limb or organ is threatened. Tissue plasminogen activator (tPA) should be used for thrombolysis
- Thrombectomy may be considered in life threatening venous thrombus - vascular surgery opinion may be sought
- Vena caval filter may be considered in children more than 10 kg with significant risk of embolism and anticoagulation is contraindicated; interventional radiology opinion may be sought.

**Renal Vein Thrombosis (RVT)**

- For unilateral RVT with no extension to IVC and no renal impairment, radiologic monitoring may be undertaken; anticoagulation is commenced when extension of clot is noticed. Otherwise anticoagulation should be commenced with unfractionated Heparin or LMWH
- For unilateral RVT with extension to IVC therapeutic anticoagulation should be undertaken with LMWH or unfractionated heparin.
- For bilateral RVT with renal impairment therapeutic anticoagulation should be undertaken with LMWH or unfractionated heparin.  
Initial thrombolysis with low dose tPA may be considered (see arterial thrombosis guideline for use of tPA)

**Thromboprophylaxis for CVAD**

- For children with short- or medium-term CVADs, use of routine systemic thrombo-prophylaxis is not recommended.

**Unblocking CVAD**

- To unblock CVAD, Urokinase (5000 units /ml) 0.5-1ml can be used depending on the size of the CVAD; Can be repeated if not unblocked, in 30 minutes.

## Arterial thrombosis

- Remove arterial catheter, if in situ.
- Commence iv **Heparin** (Target APTT ratio 2.0-2.5) (reversal of occlusion occurs in 70%). Arterial spasm resolves in <12 h.
- **No palpable pulse** → Assess clinical situation → d/w Consultant; seek haematology advice if available.

### If decision is to commence tPA

- Exclude ICH, recent surgery, ↑BP, HIE in last 7days
- Administer IV Vitamin K, correct thrombocytopenia, Maintain fibrinogen level >1mg/ml, Platelet >100  
FFP supplementation 10mls/kg prior to tPA infusion  
Ensure adequate access for treatment and blood sampling

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*Start tPA infusion: 0.3-0.5mg/kg/h i.v. for 6 hours only (standard dose)  
Or 0.1mg/kg/h for 24 h (low dose)*

Heparin infusion 10U/kg/h concurrently.

Check FBC & Coagulation 4 -6 hrly

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Stop tPA; ↑ Heparin infusion (no bolus) for therapeutic APTT ratio. Optimal duration of Heparin treatment is unknown.  
Adverse effect: Minor bleeding (30%) from venepuncture sites & epistaxis; Major bleeding requiring transfusion (10%)  
ICH in premature infants (13.8%)

*T/t for major bleeding (↓Hb > 2gm/dl): **Stop tPA & Heparin;***

*Cryoprecipitate 5-10mls/kg*

*Packed Red Cells & Platelets*

Life threatening haemorrhage: Factor VII<sub>a</sub> (FFP if VII<sub>a</sub> not available) + Tranexamic acid 10 mg/kg bolus.

- **Monitoring** : Check for palpable pulse + BP (pre-procedure level) → treatment end point - stop infusion of tPA.  
No palpable pulse after prescribed duration of tPA treatment → Doppler US & d/w consultant  
Administer Heparin alone for 24 h before re-administration of tPA  
Discuss with haematologist before recommencing tPA / Administer bolus of FFP before commencement of tPA

In acute severe limb-threatening ischaemia, seek opinion from vascular surgeons for consideration of thrombectomy

S Manna, 24.03.2012  
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References: 1. Albigetti M. Thromb res 2006: 118: 95-105  
2. Kotsakis A et al. J Crit Care: 2005: 373-380  
3. Monagle P et al. Chest 2012: 141: e737S-e801S