



CLINICAL GUIDELINE	
Thromboembolic Disorders	
Scope (Staff):	Nursing and Medical Staff
Scope (Area):	NICU KEMH, NICU PCH, NETS WA
<p align="center">Child Safe Organisation Statement of Commitment</p> <p>CAHS commits to being a child safe organisation by applying the National Principles for Child Safe Organisations. This is a commitment to a strong culture supported by robust policies and procedures to reduce the likelihood of harm to children and young people.</p>	

This document should be read in conjunction with this [DISCLAIMER](#)

Thrombosis in the neonate is an uncommon complication and occurs most often in premature (incidence of 6.8/1000 admissions <32 weeks) and other high-risk infants. It frequently involves arterial, larger vessels or may be related to indwelling venous or arterial catheters (10% of neonates with central vascular catheters).

The fetus and newborn are more susceptible to thrombosis because of a deficiency of thrombin inhibition and relatively deficient thrombolysis. The infant is protected from thrombosis by physiologic depression of factors II, VII, IX and X but the balance favours thrombin formation over inhibition especially in the sick neonate (plasminogen, anti-thrombin and protein C may be extremely low).

The majority of thromboses in the neonatal period are related to intravenous or intra-arterial catheters.

Catheter-related factors that increase the risk of thrombosis include:

- **UVC:** large catheter size, blood vessel occlusion, infusion of hyperosmolar solutions especially parenteral nutrition, low flow of infusion fluid, polyurethane (PU)/polyvinyl chloride (PVC) catheter, degree of endothelial damage on catheter placement and prolonged duration of UVC placement.
- **UAC:** longer duration of UAC placement, presence of calcium in the UAC infusate, hypertonic solution, smaller umbilical artery calibre, manipulation and replacement of UAC, low UAC position at L3 to L4 vertebral bodies, and PVC catheter material.

Other direct **risk factors** include:

- **Neonatal:** infection, dehydration, polycythaemia (Hct>55%), fluctuations in blood pressure, hypoxia.
- **Maternal:** pre-eclampsia, diabetes mellitus, autoimmune disorders, chorioamnionitis. Certain genetic polymorphism haemostasis genes (factor XIII-Val34Leu polymorphism, PAI-1 mutation gene 4G/5G polymorphism) are associated with higher incidence of sepsis and longer hospital stay and thus contribute indirectly to thrombogenesis in sick preterm infants.

Clinical presentation

For asymptomatic catheter-thrombosis: supportive care and close monitoring of thrombus size. If thrombus extends, treatment with anticoagulation or fibrinolytic therapy is recommended.

For symptomatic thrombosis: treatment recommended.

Site/ Type	Clinical features	Diagnosis	Management <i>Individualised (risk vs benefit)</i>
UVC thrombosis	Persistent +ve blood cultures from catheter, thrombocytopenia, line dysfunction Bilateral lower limb edema with IVC thrombus	Doppler USG (DUSG- safest and widely used) Venogram (gold standard), MR venogram (pelvic and intra-abdominal venous thrombus)	Removal of UVC after 3-5 days of therapeutic anticoagulation (American college of chest physicians); LMWH/UFH for 6 weeks -3 months
UAC thrombosis	Aortic and renal arterial involvement Lower limb ischemia, impaired renal function, hypertension, congestive heart failure and NEC	DUSG (preferred) Contrast angiography (gold standard),	Remove catheter, anticoagulation with UFH/LMWH, fibrinolytic therapy, surgery (if life/ limb threatening)
PICC lines/ long lines	Depends on device location and size Upper venous system thrombosis- SVC syndrome (swelling, pain, discolouration of upper limbs, chylothorax, chylopericardium) Right atrial placement- intracardiac thrombus (new onset murmur, unresolving sepsis, thrombocytopenia, heart failure) and embolic complications	CXR, AXR and echocardiography	Remove PICC line after 3-5 days of therapeutic anticoagulation
Renal vein thrombosis	Most common non catheter associated thrombosis (present in- utero, by 72 hrs of life or around four weeks of life); maybe associated with adrenal hemorrhage Flank mass, hematuria, thrombocytopenia	DUSG	Unilateral without renal insufficiency and no IVC extension: LMWH/ supportive management Bilateral RVT, associated renal insufficiency OR IVC extension: LMWH (no/mild renal insufficiency), UFH (severe renal impairment), consider concomitant fibrinolysis
Peripheral arterial line (PAL)	Limb oedema, pallor or cold extremities distal to cannulation site, weak/ absent pulse, reduced or immeasurable BP	DUSG	Remove catheter, topical nitro-glycerine, anticoagulation with UFH, rarely surgical thrombectomy and microvascular repair
Arterial ischemic stroke	Additional risk with foetal heart abnormalities, twin to twin transfusion syndrome, hypoglycaemia and maternal antiphospholipid antibody syndrome and placental abnormalities Presents as- apnoea, seizures, poor feeding, abnormal tone	Bedside cranial USG (sensitive 16-70%), first week of life MR angiogram	Antithrombotic therapy - controversial Supportive treatment in acute phase (fluid balance, anti-seizure medications, ventilation) Initiate UFH/LMWH (with cardio-embolic source) Recurrent stroke- aspirin and anticoagulation therapy.
Portal venous thrombosis (associated with UVC), right atrial thrombosis, cerebral sino-venous thrombosis and spontaneous aortic thrombosis are rare events in neonates			

The classical clinical presentation of homozygous protein C or S deficiency is with cerebral or ophthalmic damage occurring **in utero**, purpura fulminans within hours of birth (acute lethal form of DIC with skin necrosis from dermal vasculature thrombosis) and rarely large vessel thrombosis. The diagnosis requires the clinical picture and undetectable levels of protein C/S as well as heterozygous levels in the parents.

- Treatment for these disorders is with FFP 10-20 mL/kg every 6-12 hours. Protein C concentrate is also available. Treatment should continue until all the manifestations resolve. Long term therapy with warfarin aims to keep the INR 2.5-4.5 but the effect on bones of long term warfarin beginning in infancy is not known.

Laboratory Tests

- In addition to diagnostic imaging (**including cranial ultrasound**), baseline laboratory tests in the neonate before initiation of any therapy should include: platelet count, prothrombin time, activated partial thromboplastin time (aPTT) and fibrinogen concentration.
- Maternal blood should be tested for lupus anticoagulant and anticardiolipin antibody.
- Evaluation for prothrombotic disorders (panel including antithrombin/AT-III, protein C and S, Factor V Leiden, homocysteine and prothrombin 20210 mutation) should be conducted in newborns with thrombosis which is clinically significant, recurrent or spontaneous following the guidelines set by the Subcommittee for Perinatal and Pediatric Thrombosis of the Scientific and Standardization Committee of the International Society of Thrombosis and Hemostasis (*Manco-Johnson, 2002*), but the timing of this evaluation may better be left (discuss with haematology) until the acute clinical event has resolved. The results must always be interpreted in the light of age-appropriate normal ranges and laboratory-specific reference ranges. Whether newborns with catheter-related thrombosis require these studies is uncertain.
- Testing can be deferred if blood sampling is difficult because the results will not affect therapy, although they may affect the risk of recurrent thrombosis. Alternatively, these conditions can be excluded by testing the parents.
- Tests that are abnormal in the newborn should be repeated within 6–8 weeks.
- Both parents should be tested for the prothrombotic state if the results of the newborn's tests are abnormal, as this will help to distinguish acquired from congenital deficiencies.
- There is no data to support screening for thrombophilias in neonates without clinical evidence of thrombi. Use of these screening tests for non-specific symptoms (e.g. neonatal seizures) should be performed under the auspices of a clinical research protocol.
- During anticoagulant treatment, maintain platelet count >50,000/ microL and fibrinogen >100mg/dL. Duration of anticoagulant therapy depends on clinical course; if thrombus resolves (10-14 days); if thrombus persists (up to 3 months).

Treatment of Major Thrombi

1. **Heparin Anticoagulation (UFH: unfractionated heparin, LMWH: low molecular weight heparin)**

LMWH preferred (to UFH) as can be administered subcutaneously and require minimal monitoring and dose adjustment. LMWH also has reduced risk of immune-mediated thrombocytopenia and osteoporosis.

Anti-Xa level (target between 0.3-0.7 U/ml) is better than APTT for monitoring as the APTT is frequently prolonged in sick neonates.

Refer to Neonatal Medication Protocol – [Heparin Sodium](#)

2. Others (not used in neonates)

- Factor Xa inhibitors (fondaparinux, rivaroxaban, apixaban and edoxaban)
- Direct thrombin inhibitors(argatroban, bivalirudin and dabigatran)

3. Long Term Anticoagulation (Warfarin, Aspirin, Clopidogrel)

Rarely required except for those with homozygous or multiple thrombophilia traits or congenital cyanotic heart disease who may need life-long anticoagulation.

4. Thrombolytic Therapy (r-TPA/ recombinant tissue plasminogen activator)

This is reserved for recent arterial thromboses that compromise perfusion.

Thrombocytopenia (<100,000/microL), low fibrinogen (<100mg/dL) and severe coagulopathy to be corrected before treatment

Contraindications to treatment: major surgery or haemorrhage in previous 10 days, neurosurgery within three weeks, severe asphyxia event within seven days, invasive procedure within previous three days, seizures within 48 hrs, prematurity<32 weeks, systemic sepsis, active bleeding or inability to maintain platelets >100,000/microL or fibrinogen >100mg/dL

Recombinant tissue plasminogen activator (rt-PA) is available and is given at 0.1-0.6 mg/kg/hr (without a loading dose) over 6 hrs. Transfusion of 10 ml/kg of FFP prior to r-TPA increases incidence of clot resolution by providing adequate plasminogen levels.

Streptokinase and Urokinase- very rarely used in neonates.

5. Nitro-glycerine patch

Apply to contralateral limb in peripheral vasospasm post insertion of UAC or PAL.

Related CAHS internal policies, procedures and guidelines

Neonatal Medication Protocol – [Heparin Sodium](#)

References and related external legislation, policies, and guidelines

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