Yorkshire and Humber ODN (SOUTH)
Network Clinical Guideline

Title: Management of a neonate at risk of being affected with a congenital bleeding disorder

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Date Ratified: TBC

This clinical guideline has been developed to ensure appropriate evidence based standards of care throughout the North Trent Neonatal Network. The appropriate use and interpretation of this guideline in providing clinical care remains the responsibility of the individual clinician. If there is any doubt discuss with a senior colleague.

Best practice recommendations represent widely used evidence-based practice and high quality standards that all Neonatal Units across the Network should implement. Subsequent suggested recommendations may be put into practice in local units. However, alternative appropriate local guidelines may also exist.

1. Background.
   Neonatal bleeding disorders are rare, and often diagnosed after the neonatal period. Some infants will be known to have a diagnosis (as a result of antenatal screening) or be potentially affected as a result of a family history of bleeding disorder.

2. Aim
   The guideline is intended for use in the management of neonates who are known to have, or who are at risk of being diagnosed with, a congenital bleeding disorder, who are born at the Jessop Hospital for Women, Sheffield. It is for guidance in the management of neonates born elsewhere.

3. Areas outside remit
   Infants with disseminated intravascular coagulation and other acquired coagulopathies are not covered by this guideline.

4. Core Guideline (Index)

4.1 Diagnoses
Moderate/Severe Bleeding disorders:
Moderate/severe haemophilia A (FVIII <0.05iu/ml)
Moderate/severe haemophilia B (FIX <0.05 iu/ml)
Type 2 and Type 3 Von Willebrand's disease
Rare severe congenital factor deficiencies e.g II, V, VII, X, XIII
Severe platelet function defect e.g Glanzmann's thrombasthenia, Bernard Soulier Syndrome.

Mild Bleeding disorders
Mild Haemophilia A (FVIII >0.05iu/mL)
Mild Haemophilia B (FIX >0.05iu/mL)
Female carriers of haemophilia A or B [may have low FVIII or FIX levels]
Type 1 von Willebrand disease
Factor XI deficiency (variable bleeding phenotype)
Mild deficiencies of other congenital factor deficiencies eg II, V,VII, X, XI, XIII
Mild Platelet function disorders (eg storage pool disease)

4.2 Labour and delivery
When it is known that the mother is a carrier for one of these conditions, an antenatal and delivery plan will be agreed between the haematologist and the obstetrician caring for the mother. A written plan should be available in the mother's notes.
Antenatal care and delivery of a neonate potentially affected with a severe bleeding disorder should be arranged at the Jessop Wing with involvement of the haemophilia clinicians at STH, where specialist coagulation factor investigations can be undertaken in a timely fashion. Such patients should be seen at the joint haematology/obstetric clinic at Jessop Wing.

4.3 Diagnosis.
Where a diagnosis of a severe coagulation factor deficiency is considered (see appendix 1), cord blood samples should be taken as indicated at delivery (citrated- blue top bottle filled to the line) and sent with a request form for the appropriate urgent investigation to the coagulation laboratory at STH. This request should be discussed with the coagulation laboratory (ext 12955 or bleep out of hours). Results will be available the same day (usually within a few hours) and if abnormal should be discussed with the haematology ST or Haemophilia consultant on-call at STH.
Where a diagnosis of a severe platelet function defect is considered (see appendix 1), a purple EDTA cord blood sample should be taken and sent to haematology laboratory at STH for FBC and glycoproteins- discuss with hematology SpR or Haemophilia consultant on call at STH.

4.4 Management of bleeds
Any bleeding including cephalohaematoma should be discussed promptly with the STH haematology ST or Haemophilia consultant on-call since prompt factor replacement is likely to be indicated.

4.5 Vitamin K
Vitamin K should be given by the oral route if at risk of a moderate/severe bleeding disorder (See appendix 1). Once results are available, if baby unaffected, can have an IM dose prior to discharge.

4.6 Cranial imaging
Where indicated (see Appendix 1), a cranial ultrasound scan should be undertaken on the next working day to assess for any intracranial haemorrhage. Any abnormality on the cranial ultrasound should be discussed with the STH haematology ST or Haemophilia consultant on-call so that bleeds are treated promptly.

Urgent CT/MRI scanning should be considered if there is suspicion of a bleed on the ultrasound scan, or should there be symptoms or signs suggestive of an intracranial haemorrhage.

If there is clinical concern regarding a possible intracranial haemorrhage this should be discussed as an emergency with the STH Haemophilia consultant so that immediate treatment can be arranged. Treatment should not be delayed whilst waiting for definitive imaging studies. A cranial USS may be the most immediately available form of imaging but if there is clinical concern of a bleed consideration should be given to more detailed imaging.

4.7 Prophylaxis with clotting factors

Short-term prophylactic clotting factor treatment with the intention of reducing the risk of intracranial haemorrhage associated with delivery should be considered in neonates with severe bleeding disorders (see Appendix 1) with one or more the following risk factors:

1. prematurity (<36 weeks)
2. instrumental delivery
3. prolonged second stage of labour i.e. active pushing (Primigravida >2hrs; Parous >1hr)
4. superficial cranial bruising

Advice should be taken from the Haemophilia consultant on call.

Prophylaxis regime.
Where prophylaxis is indicated, at least 2 doses, each of 250 units factor VIII or IX, will generally be given for severe haemophilia A or B respectively. Where indicated, the first dose should be given as soon as possible following delivery after confirmation of the diagnosis. Alternate day dosing will generally be adopted for neonatal prophylaxis.

4.8 Clinical review

The initial diagnostic work up and immediate management will be coordinated by the Haemophilia consultant at STH.
When a baby is found to be affected with a congenital bleeding disorder the paediatric haematology consultant at Sheffield Children's Hospital should also be informed.
Factor concentrate, and advice on administration, will be provided by the Haemophilia team at the Royal Hallamshire Hospital.
Where possible, when a neonate has been diagnosed with a moderate/ severe bleeding disorder, clinical review will be undertaken by the STH Haemophilia consultant/Haematology ST and Dr Jeanette Payne (consultant paediatric haematologist, Sheffield Children's Hospital) and a joint treatment plan agreed. If Dr Payne is unavailable ongoing care will be provided by the STH Haemophilia team.

Where possible Shaun Emmitt or Louise George (Haemophilia Specialist Nurses, Sheffield Children's Hospital) will visit the parents of neonates diagnosed with a moderate/ severe bleeding disorder to provide support and information and contact details prior to discharge.

4.9 Follow-up

All neonates with confirmed congenital bleeding disorders or where the diagnosis has not been excluded (e.g type 1 VWD, mild haemophilia) should be formally referred at discharge to Dr Jeanette Payne, Sheffield Children's Hospital and will be seen as in Appendix 1.

4.10 Immunisations

For neonates affected with congenital bleeding disorders the parents and GP should be advised that immunizations should be given by the subcutaneous route.

4.11 Contact details

Sheffield Haemophilia Centre (Royal Hallamshire Hospital) ext 0114 2713211
(working hours only 8-5pm Mon - Fri)

Coagulation Laboratory (Royal Hallamshire Hospital)
0114 2712955
Out of hours bleep via switchboard

Sheffield Teaching Hospital Haematology ST and Haemophilia Consultant- contactable via switchboard (0114 2434343)-.

Consultants: Dr Mike Makris
Dr Rhona Maclean
Dr Joost van Veen
Dr Eddie Hampton
Dr Giorgia Saccullo

Sheffield Children's Hospital
Paediatric Haematology consultant on-call- contact via switchboard

Dr Jeanette Payne ext 0114 2717477/0114 2717349, bleep via switchboard
Shaun Emmitt and Louise George Haematology Specialist Nurses ext 0114 2717329, bleep via switchboard

5. References

Chalmers, E., Williams, M., Brennand, J., Liesner, R., Collins, P.m Richards, M. and on behalf of the Paediatric Working Party of the United Kingdom Haemophilia Doctors' Organisation (2011), Guideline on the management of haemophilia in the fetus and neonate. British Journal of Haematology, 154: 208-215

Pavord S, Rayment R, Madan B, Cumming T, Lester W, Chalmers E, Myers B, Maybury H, Tower C, Kadir R on behalf of the Royal College of Obstetricians and Gynaecologists. Management of Inherited Bleeding Disorders in Pregnancy. BJOG 2017; 124:e193-e263

Appendix 1: Management of neonates potentially affected by inherited bleeding disorders after delivery

*Coagulation factor levels should be interpreted against age adjusted reference ranges

Neonate at risk of:	Cord blood (test at birth)?	Cranial Ultrasound?	Vitamin K	Primary prophylaxis?	To be seen at SCH
Severe/ Moderate Haemophilia A or B	Yes for male babies only	Yes, if diagnosed with severe haemophilia. Consider MRI if symptoms or signs suggestive of ICH.	Male babies only- Oral vitamin K. Once results available, if unaffected, give IM vitamin K before discharge.	Consider if affected and increased risk of bleeding due to trauma at delivery or prematurity	Urgent referral if affected. See before discharge. Female Neonates: Potential carriers – refer to SCH at discharge. Will see at any time if symptomatic/ need surgery otherwise will see at school age.
Mild Haemophilia A or B	Males only Haem A- cord blood ok Haem B- venepuncture post Vit K preferable	No	Male babies only- Oral vitamin K. Once results available, if unaffected, give IM vitamin K before discharge.		Refer if low levels. Timing of review will depend on level compared with age appropriate normal range
Type 3 von Willebrand Disease	Yes	Yes, if diagnosed with Type 3 vWD. Consider MRI if symptoms or signs suggestive of ICH.	Oral vitamin K. Once results available, if unaffected, give IM vitamin K before discharge.	Consider if affected and increased risk of bleeding due to trauma at delivery or prematurity	Urgent referral if affected. See before discharge
Type 2 von Willebrand Disease	Yes	Not routinely	Oral vitamin K. Once results available, if unaffected, give IM vitamin K before discharge.		Refer at discharge. If affected will be seen soon. If normal results will see from 6m for repeat
Type 1 von Willebrand Disease	No	No	Intramuscularly	No	Refer at discharge. Will see from 1yr onwards unless symptomatic/need for surgery Routine screen around school age
Factor XI deficiency	No, (unless at risk of homozygosity or compound heterozygosity)	No	Intramuscularly unless severe deficiency	No	Refer at discharge. Will see from 1yr onwards unless symptomatic/need for surgery Routine screen around school age
Other factor deficiencies: Fibrinogen (associated with bleeding) II, V,VII, X, XIII, V+VIII combined	Yes (if thought at risk of severe deficiency), Otherwise No	Yes, if diagnosed with severe factor deficiency. Consider MRI if symptoms or signs suggestive of ICH.	Oral if considered to be at risk of severe deficiency (see delivery plan). IM in all others	Consider if affected and increased risk of bleeding due to trauma at delivery or prematurity	Urgent referral if severely affected. See before discharge Refer to SCH at discharge. Will see mildly affected at any time if symptomatic/ need surgery otherwise will see at school age.

Neonate at risk of:	Cord blood (test at birth)?	Cranial Ultrasound?	Vitamin K	Primary prophylaxis?	To be seen at SCH
Bernard-Soulier Syndrome	Yes if at risk of being severely affected (glycoproteins and FBC)	Yes if affected	Oral vitamin K if at risk of being severely affected. Once results available, if unaffected, give IM vitamin K before discharge.	No	Urgent referral if affected. See before discharge
Glanzmann's thrombasthenia	Yes if at risk of being severely affected (glycoproteins) Measure platelet count If maternal alloimmunisation, there is risk of fetal thrombocytopenia and neonatal ICH Repeat platelet count d3-5 if at risk thrombocytopenia	Yes if affected	Oral vitamin K if at risk of being severely affected. Once results available, if unaffected, give IM vitamin K before discharge.	Platelets if <30	Urgent referral if affected. See before discharge
Other platelet function defects	No	No	intramuscular	No	Refer to SCH at discharge. Will see at any time if symptomatic/ need surgery otherwise will see at school age.