

# Management of Newborns of Haemophilia Carriers or other Bleeding Disorders.

## Introduction

This will most commonly relate to mothers known to be carriers of haemophilia A or B where the x-linked recessive nature of the inheritance means that boys will have a 50% chance of being affected. However about 30% of cases of haemophilia will be new mutations and there will be no family history. So it is a diagnosis that should be considered in any baby boy with unusual bleeding.

Severe disease can be excluded by assaying cord blood for inherited bleeding disorders. This is recommended in the guidelines of the Haemophilia Centre Doctors Organisation in the United Kingdom.<sup>1</sup> However, its value in milder disease (particularly haemophilia B) is controversial, and results should be confirmed by peripheral blood testing. In addition, adult levels of vitamin-K-dependent clotting factors and factor XI may not be present until after 6 months of age.

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## Risks and Consequences of Neonatal Haemophilia:

In general terms, baby boys of known haemophilia carriers should be assumed to have haemophilia until proven otherwise. Specifically this relates to avoidance of anything that could precipitate bleeding such as intramuscular injections or elective surgery such as circumcision. The major risk of neonatal haemophilia is intracranial haemorrhage.

Prophylactic factor replacement therapy should not be routinely given and may be associated with an increased risk of inhibitor development in children with haemophilia (inhibitor development is an immune response inhibiting factor replacement from stopping a bleeding episode).<sup>1-3</sup> Similarly, the use of prophylactic recombinant factor VIIa has not been shown to improve clinical outcomes.<sup>2</sup>

In neonates with haemophilia or severe subtypes of von Willebrand disease, vitamin K should be given orally or subcutaneously.<sup>1</sup> Immunisation should be given subcutaneously or intradermally.<sup>1,2</sup>

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## Neonatal Haemophilia and Cranial Haemorrhage:

The major risk for haemophiliac newborns is intracranial and extracranial haemorrhage. This is estimated to occur in around 4% in newborns with severe haemophilia.<sup>1,4,5</sup> Kulkarni et al reviewed the case series in the literature and reported an incidence of 3.6% of which 65% were intracranial and 35% extracranial (subgaleal or cephalohaematoma). The mean age at presentation was 4.5 days but with a wide range from birth to 28 days. Because presentation may be delayed, mothers should be made aware of potential symptoms, such as vomiting, seizures and poor feeding.<sup>6</sup>

Pre-delivery ultrasound determination of the sex of the fetus is useful, because female infants do not usually have an elevated risk of cranial haemorrhage. The risk of cranial haemorrhage is also increased in neonates with severe forms of von Willebrand disease,<sup>7</sup> but is very rare in infants with factor IX deficiency.<sup>8</sup>

The Australian Haemophilia Centre Directors Organisation (AHCDO) recommends that neonates with a bleeding disorder should have a cerebral ultrasound examination soon after birth to check for intracranial haemorrhage.

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# Practical Management in Babies at risk of Haemophilia:

## **Diagnosis:**

- In babies of known haemophilia carriers, cord blood should be taken for measuring factor VIII or factor IX levels. These assays can be performed in the RPAH lab during normal working hours. Depending which scientist is on duty, it may be possible to arrange these assays during daylight hours over the weekend but they cannot be performed at night. Phone the Haematology lab on extension 58515 for information
- If the blood cannot be assayed for clotting factor levels in a timely manner, then normal coagulations studies can be helpful in excluding **severe** haemophilia where the APPT will almost always be prolonged beyond 60 seconds (NB. Term neonates may have an APPT up to 45 secs). Note, this does not exclude milder forms of the disease.

## **Precautions:**

Until the coagulations status of an at-risk baby is known:

- Intramuscular injections should be avoided. Vitamin K should be given orally and immunisations such Hepatitis B should be given subcutaneously.
- Take care with peripheral blood sampling; particularly dont squeeze the heel too hard with heel prick sampling.
- In babies shown to have haemophilia, a routine formal cerebral ultrasound examination to check for intracranial haemorrhage should be considered soon after birth on day 2 or 3, or earlier if cranial trauma/difficult delivery.
- Babies with proven or probable severe forms of Haemophilia should have 4-6 hourly routine observations during their hospital stay.
- There should be a high index of suspicion for intra-cranial haemorrhage and all at-risk neonates should be carefully observed for signs of ICH including any abnormal neurology, lethargy, poor feeding, apnoea, vomiting and a tense anterior fontanelle. There should be a very low threshold for arranging a cerebral ultrasound if there is clinical concern.
- Haemophilia associated ICH is reported up to 28 days<sup>6</sup> so parents should be advised about possible signs or symptoms.
- Prophylactic factor replacement should not be given, even in neonates known to have a severe bleeding disorder, because of the potential risk of inhibitor development.

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## Management of bleeding in Haemophiliac newborns

- Local advice may be sought from the Haemophilia clinic (57013) or Dr Scott Dunkley or the Coagulation Registrar. In addition, it is also advisable to discuss the situation with a Paediatric Haematologist at either Childrens Hospital Westmead or Sydney Childrens Hospital.
- Neonates known (or suspected) to have haemophilia A or B, and who have evidence of either intracranial bleeding or severe bleeding elsewhere, should receive immediate factor replacement with recombinant factor VIII or IX, respectively.<sup>1,4,9</sup>
- If haemophilia is suspected in a neonate with bleeding, but the type of haemophilia is unknown, both factor VIII and IX should be given until confirmation of specific factor levels.
- Neonates with severe haemophilia A or B and severe bleeding require 100% plasma factor levels. This can be achieved by giving, as appropriate, 75 IU/kg recombinant factor VIII or 150 IU/kg

recombinant factor IX.

- Ensure blood is taken for Factor VIII and IX assays prior to giving any replacement clotting factors. At RPAH, factor VIII and IX assay can be obtained from Haematology with a routine coagulation studies tube provided to the haematology laboratory.
- Factor is kept in the Haemophilia clinic fridge and can be accessed after-hours through NARMU. Factor levels should be maintained in the normal range for at least 710 days, and a haemophilia specialist in a paediatric haemophilia treatment centre should coordinate therapy.
- In babies with severe persistent bleeding, consider the possibility of a secondary consumptive coagulopathy with will need managing by more general factor replacement with fresh frozen plasma or cryoprecipitate.

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## Referral:

Neonates with an identified inherited bleeding disorder should be referred to a paediatric haemophilia treatment centre at either the Childrens Hospital Westmead or Sydney Childrens Hospital.

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## Key Points

Key Point	Level of Evidence
Take cord blood for Factor VIII or IX assay. If after hours, check APPT, >60 seconds suggests severe haemophilia.	4
Give Vitamin K orally and Hepatitis B vaccine subcutaneously.	4
Arrange cerebral ultrasound on day 2 or 3 to rule out intracranial haemorrhage.	5
Observe all affected babies closely for symptoms or signs of intracranial haemorrhage.	5

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## References

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