



CLINICAL GUIDELINE

Anaemia and Bleeding Disorders

Scope (Staff):	Nursing and Medical Staff
Scope (Area):	NICU KEMH, NICU PCH, NETS WA

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

Causes of Anaemia

1. Early onset within the first week (Acute or chronic blood loss).
2. Later onset after the first week (Decreased red cell production and/or shortened red cell survival).

In normal healthy newborns haemoglobin levels decrease from a mean of 19.3 g/dl at birth to a nadir of 10.7 g/dl (8.9-12.5) at 9 weeks. The Hb levels of preterm infants are only slightly lower than full term infants however the nadir occurs earlier and is lower.

Early Onset

- Haemolytic disease.
- Fetomaternal.
- Twin to twin transfusion - donor.
- Subgaleal haemorrhage.
- APH - Placenta Praevia, Abruption, Velamentous cord insertion / cord rupture.
- Hepatic rupture.
- Congenital infections i.e. CMV.
- Deceased twin - disseminated intravascular coagulopathy (DIC).
- Isoimmunisation ~ Rhesus disease / ABO incompatibility.

Later Onset

- Iatrogenic blood loss from frequent blood sampling.
- Sepsis, NEC.
- Anaemia of prematurity.
- Haemoglobinopathies.
- Haemorrhagic disease - Vitamin K deficiency, Thrombocytopenia.
- Hereditary spherocytosis.

History

A detailed history is essential. Family and obstetric history may reveal a familial bleeding disorder (haemophilia, rare autosomal recessive platelet function disorders or

thrombocytopenia-maternal ITP or alloimmune thrombocytopenia with a previously affected sibling).

Laboratory Tests

- Full Blood count and film.
- Group and Direct Coombs (Antiglobulin test).
- Maternal Kleihauer (Determination of fetal haemoglobin in maternal circulation).
- Exclude Haemoglobinopathies.
- SBR.
- Coagulation studies. (Normal neonates have a prolonged APTT, especially if preterm, and often the test is not helpful). Factor assays will be more useful for suspected haemophilia.
- Check stools for occult blood if applicable.

While new whole blood platelet factor analysers (PFA) may help diagnose the rare infant with a platelet function defect, in general these disorders and von Willebrand's disease are easier to determine at 6-12 months of age.

Haemoglobin threshold for preterm infants

In the absence of clear evidence from high-quality trials, the clinical/consumer reference group (CRG) provides the following clinical guidance for transfusion in preterm infants.

Post-natal week	Hb (g/L)	
	No Respiratory Support	Respiratory support (e.g. Supplemental oxygen, high flow, CPAP, Positive pressure ventilation)
1	100-120	110-130
2	85-110	100-125
>3	70-100	85-110

Table adapted from Patient Blood Management Guidelines: Module 6 (2016)

The threshold for transfusion within these ranges may be influenced by the presence of symptoms and other factors such as:

- anticipated blood loss (e.g. haemolysis or surgery)
- Quality of nutrition
- Severity of illness
- Site of sampling

Critical Bleeding Protocol

Activate [Critical Bleeding Protocol](#) if the estimated blood loss is >40mL/kg with shock and laboratory or clinical evidence of coagulopathy.

See [Exchange Transfusion](#) for severe haemolytic anaemia.

Iron Deficiency Anaemia

Term infants generally have sufficient iron stores to meet their requirements for the first 4–6 months of life. Preterm and low birth weight infants Neonatal iron stores are largely laid down during the third trimester of pregnancy, hence most preterm infants are at risk of subsequent iron deficiency.

Iron supplementation should begin in infants born < 35 weeks gestation and greater than 4 weeks postnatal age, and fed unfortified breast milk. Preterm infants have a daily requirement of 2–3 mg/kg/day of elemental iron, which can usually be met by iron supplementation until there is adequate dietary iron intake. Refer to [Ferrous Sulphate](#) protocol for iron supplementation.

Bleeding Disorders

Normal haemostasis requires vascular integrity, normal platelet function and a functioning coagulation system.

Thrombocytopenia

15% of neonatal patients have a thrombocytopenia of between 100-150,000. Counts below 50,000 should be considered for investigation.

Bleeding may occur with trauma with platelet counts below 50-70,000. Spontaneous bleeding can occur with counts below 20,000. Infants with invasive lines and receiving intensive care procedures may need to be transfused with platelets earlier than well infants.

Bleeding is more likely at any given thrombocytopenic level if the cause is decreased production or there is an associated platelet function defect.

Causes

- Immune - Alloimmune thrombocytopenia (FMAIT), maternal immune thrombocytopenia (ITP).
- Sick infant - sepsis, viral infection (TORCH), NEC, DIC, hyper-viscosity, RDS.
- Congenital - Kassabach-Merritt Syndrome, Type 2b von Willebrand disease, trisomy 13, 18, 21, autosomal disorders.

Key Points

- Platelet count may quickly drop over the first few days of life.
- Thrombocytopenia may last several weeks.
- Parents need to know if subsequent pregnancies may result in a severely affected fetus requiring monitoring and treatment during their next pregnancy.

Treatment

- Discuss with the haematologist on call who will review the blood film for the size of the platelets (larger platelets are usually younger platelets and indicates increased turnover rather than decreased production) and to look for any clots.

- Review maternal platelet count, history. Consider NAIT and type the parents' platelets. See below for further information on NAIT.
- If platelets <20,000-30,000 (well infant) or <50,000 (sick infant) transfuse CMV negative platelets (all platelets are now irradiated and collected with a filter so washing is not required). If NAIT is likely (well infant and marked thrombocytopenia, request PLA1a negative platelets until the parents platelet typing is known.
- Head ultrasound to look for any intra cranial bleeding.
- Bone marrow analysis may be required in refractory thrombocytopenia and to look for rare congenital causes of thrombocytopenia.

Platelet Count (x10 ⁹ /L)	Indication to trigger platelet transfusion in neonates
<30	<ul style="list-style-type: none"> • Known or suspected fetal & neonatal alloimmune thrombocytopenia (NAIT) in term infant (PBM:6) • Stable term or preterm neonate with asymptomatic thrombocytopenia and no bleeding
30 – 50	<ul style="list-style-type: none"> • Preterm neonate with thrombocytopenia being treated for sepsis or requiring respiratory support
<50	<ul style="list-style-type: none"> • Known or suspected fetal & neonatal alloimmune thrombocytopenia (NAIT) in preterm infant (PBM:6) • Other sites of bleeding (excluding intracranial) • Term or preterm neonate with bleeding symptoms (mucocutaneous, gastrointestinal, petechiae/purpura), coagulopathy prior to surgery
<100	<ul style="list-style-type: none"> • Intracranial bleeding • Term or preterm neonate with major bleeding (drop in Hb requiring RBC transfusion) or those that require major surgery (e.g. neurosurgery)

Fetomaternal or Neonatal Allo-immune Thrombocytopenia (NAIT)

(Adapted from Patient Blood Management Guidelines: Module 6)

A rare but potentially serious condition that causes bleeding in the newborn is Fetomaternal or neonatal allo-immune thrombocytopenia (FMAIT or NAIT). This condition is the platelet equivalent of haemolytic disease of the newborn.

The fetus and newborn are at risk of thrombocytopenia and intracranial haemorrhage and bleeding in newborn. Untreated FNAIT is associated with a high rate of intra- cranial haemorrhage (~25%).

Incidence: 1:2000 to 1:3000 live births among Caucasians. NAIT often (>60%) occurs during the first pregnancy.

NAIT is caused by maternal IgG alloantibodies against a fetal platelet specific alloantigen in the Human Platelet Antigen (HPA) system.

- 75% of cases in a Caucasian population are caused by anti-HPA-1a and 20% by anti-HPA-5b.
- In oriental populations, anti-HPA-4b is more common than anti-HPA-1a.

There may or may not be a history of thrombocytopenia in a previous infant.

Investigations

- Maternal serum is the test sample usually required for the investigation of possible NAIT.
- Currently the tests are done at FSH and the details are given at under platelet antibody investigations. Link to form <http://wspwvmfts01/Fasttrack/Portal/FRM-1010.doc>
 - For urgent contact phone 61528005.
- Usually the mother's serum is tested against both panel cells from known HPA-typed donors and against platelets from the father.
- Reactivity with only the father's platelets may indicate the presence of antibody directed to a low-incidence antigen.
- Antibodies to HLA antigens have also been reported to cause NAIT although the extent of their involvement is controversial.

Management of the neonate

(ALWAYS DISCUSS WITH THE HAEMATOLOGIST ON CALL)

- For neonates with known or suspected fetal and neonatal alloimmune thrombocytopenia:
 - Urgent platelet transfusion should be given if platelets are below $30 \times 10^9 /L$ in a term infant or below $50 \times 10^9 /L$ in a preterm infant, even in the absence of clinically significant bleeding
 - If there is active bleeding, a higher threshold should be considered ($100 \times 10^9 /L$ for intracranial bleeding, and $50 \times 10^9 /L$ for other sites of bleeding).
 - In all cases, a paediatric haematologist should be consulted.
- For neonates with known or suspected fetal and neonatal alloimmune thrombocytopenia, random donor platelets should be used if antigen-matched platelets are not immediately available. Continued use of random donor platelets is acceptable if antigen-matched platelets cannot be obtained. Because of short survival of random donor platelets, repeated transfusion is likely to be needed.
- For neonates with known or suspected fetal and neonatal alloimmune thrombocytopenia, platelet count response to transfusion should be checked **within 12 hours**
- For neonates with fetal and neonatal alloimmune thrombocytopenia, IVIG may be considered at a dose of 1–2 g/kg body weight. Discuss with Haematologist prior to transfusion: [Intragam](#).

Management of subsequent pregnancies

- Subsequent pregnancies should be carefully monitored as there is a risk for in-utero bleeding. **Letter to GP mentioning the potential risk for future pregnancies at the time of discharge.**
- When possible, compatible platelets should be maintained on hand at the expected delivery time.

A [Foetal Neonatal Alloimmune Thrombocytopenia \(FNAIT\) - Clinical Information](#) form needs to be completed and submitted to the Australian Red Cross (through blood bank) for all confirmed NAIT. (Sample form [Appendix A](#))

Vitamin K Deficiency

The **Classical** presentation is at 2-6 days of age in healthy full term infants and occurs because of poor placental transfer of vitamin K, low levels in breast milk and a sterile gut. It can be prevented by a single dose of 0.5 mg for infants < 1500 grams and 1 mg for infants > 1500 grams IM/IV at birth or an oral dose of 2-4 mg at birth with subsequent doses.

See Neonatal Medication Protocol: [Phytomenadione \(Vitamin K\)](#).

Related CAHS internal policies, procedures and guidelines

Neonatology Guideline

- [Critical Bleeding Protocol \(BCP\)](#)
- [Exchange Transfusion](#)

Neonatology Medication Protocol:

- [Phytomenadione \(Vitamin K\)](#)

PCH Transfusion Medicine Protocols

- [Intravenous Immunoglobulin \(IVIg\)](#)
- [Blood Products Prescription and Informed Consent](#)


WNHS Transfusion Medicine Protocol:

- [Blood Products - Checking Procedure Pre Administration](#)
- [Blood Products - Pre Transfusion Testing for Adults and Neonates](#)
- [Blood Products - Prescription Consent and Refusal](#)
- [Intragam.](#)

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Appendix A



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Foetal Neonatal Alloimmune Thrombocytopenia (FNAIT) – Clinical Information

Note: You must also complete and submit a National Platelet and Neutrophil Investigation Request Form (FRM-02189)

Patient (Maternal) Details							
Last Name				First Name			
MRN/URN				DOB			
Hospital							
Baby's last name, first name							
Paternal last name, first name				DOB			
Maternal Obstetric history							
Obstetric history	G		P		L		Any previous FNAIT affected baby? <input type="checkbox"/> Yes <input type="checkbox"/> No
Severity of previous FNAIT affected baby	<input type="checkbox"/> ICH <input type="checkbox"/> Mucocutaneous bleed/ petechiae <input type="checkbox"/> IUFD <input type="checkbox"/> Thrombocytopenia <input type="checkbox"/> GI bleed <input type="checkbox"/> Other (specify i.e. placental insufficiency/IUGR)						
Previous transfusions	<input type="checkbox"/> Yes <input type="checkbox"/> No		Maternal ethnicity			Paternal ethnicity	
Autoimmune disorder (e.g. ITP, SLE)	<input type="checkbox"/> Yes (provide details below) <input type="checkbox"/> No						
Current Pregnancy							
Date of delivery or expected date of delivery							
Complications during pregnancy	<input type="checkbox"/> Pre-Eclampsia <input type="checkbox"/> Placental abruption <input type="checkbox"/> HELLP <input type="checkbox"/> Perinatal hypoxia <input type="checkbox"/> Infection (specify below) <input type="checkbox"/> Placental insufficiency <input type="checkbox"/> Other (specify below) <input type="checkbox"/> None						
Treatment history	<input type="checkbox"/> IVIg <input type="checkbox"/> Steroids <input type="checkbox"/> Other (specify) _____						
Mode of delivery	<input type="checkbox"/> Vaginal <input type="checkbox"/> Caesarean Section <input type="checkbox"/> Instrumental Delivery						
Maternal platelet count			x10 ⁹ /L	Maternal blood group			Paternal blood group
Postnatal (Baby's history)							
Gestational age at birth			Birth weight (g)			IUGR	<input type="checkbox"/> Yes <input type="checkbox"/> No
Onset of thrombocytopenia	<input type="checkbox"/> At birth <input type="checkbox"/> Post-natal day _____						
Bleeding	<input type="checkbox"/> ICH <input type="checkbox"/> Mucocutaneous bleed/ petechiae/ purpura <input type="checkbox"/> GI bleed <input type="checkbox"/> Ventriculomegaly <input type="checkbox"/> Other (specify) _____						
Other	<input type="checkbox"/> Coagulation deficiency/defects <input type="checkbox"/> DIC <input type="checkbox"/> Other (specify) _____						
Infections (e.g. TORCH, sepsis)	<input type="checkbox"/> Bacterial (specify) _____ <input type="checkbox"/> Viral (specify) _____						
Congenital abnormality/ies	_____						
Any other relevant clinical information							
Platelet count	Initial			x10 ⁹ /L	Nadir		
	Date				Date		
Most recent			x10 ⁹ /L			Baby's blood group	
Treatment							
IVIg	<input type="checkbox"/> Yes <input type="checkbox"/> No		No. of platelet transfusions	Pooled			Apheresis
						HPA specific	
Follow up platelet counts							
		Date			Pre- transfusion (x10 ⁹ /L)	Post transfusion (x10 ⁹ /L)	

Sample form only