

Neonatal Services Guideline: Thrombocytopenia and platelet transfusion

This guideline is designed to help staff caring for babies on ward 35 Special Care Babies and the postnatal wards at the RVI. It includes a list of aetiologies to consider, suggested investigations and provides guidance on when platelet transfusion may be appropriate. There are likely to be frequent situations where alternative treatment thresholds are appropriate and referring to updates from both the Neonatal Formulary and guidelines from the British Committee on Standards in Haematology (BCSH) www.bcsghguidelines.com/ may be helpful (most recent update 2004). This guideline has been developed through consensus opinion with the collaboration of the haematologists. A list of additional references is provided at the end.

Background

Thrombocytopenia ($<150 \times 10^9/l$) is present in 1-5% of newborns and severe thrombocytopenia ($<50 \times 10^9/l$) occurs in 0.1-0.5%. The incidence is higher in NICU populations (22-35%) and in up to 50% of babies requiring intensive care.

Transfusion Thresholds

Platelet Count ($\times 10^9/l$)	Indications for Transfusion
<100	Major bleeding
<50	Confirmed or suspected NAIT +/- bleeding Clinically unstable babies with: <ul style="list-style-type: none"> • Concurrent coagulopathy • Need for surgery or exchange transfusion • Previous major bleeding
<30	All patients

The above thresholds are based on the most recent recommendations (see reference 5 below)

Transfusion Procedure

- Discuss with the consultant if the need for transfusion is not clear
- Discuss with consultant neonatologist/haematologist if neonatal alloimmune thrombocytopenia (NAIT) is a possibility or confirmed. **NAIT is potentially fatal and may require immediate intervention/early transfusion.**
- Give 20ml/kg of CMV negative platelets over 30 minutes (more quickly if very sick)
- Check compatibility by ensuring the baby's name is on the pack

See the Neonatal Formulary for further details

Causes & Timing of Onset

Early Onset (<72 hours)

Impaired platelet production due to placental insufficiency and/or fetal hypoxia is the most common cause. Many are preterm and there is frequently a history of maternal PIH. The mechanism is thought to be due to 'lineage steal' whereby pluri-potential cells are diverted down the red cell as opposed to the white cell or platelet line. Most have low platelets at birth, reach a nadir at day 4 and resolve spontaneously by 7-10 days old. Counts rarely fall below $50 \times 10^9/l$.

Severe ($<50 \times 10^9/l$) early thrombocytopenia is much less common. In sick babies with severe thrombocytopenia other mechanisms such as disseminated intravascular coagulation should be suspected. In preterm infants this is most commonly due to severe perinatal infection such as group B streptococcus, but in term infants perinatal hypoxia-ischaemia should also be considered.

When severe in an otherwise healthy term neonate, the most likely cause is neonatal alloimmune thrombocytopenia (NAIT). Discuss all these babies with Haematology (usually John Hanley).

Late Onset (> 72 hours)

After 72 hours, thrombocytopenia may be due to sepsis or NEC and may be severe and prolonged. The fall is often rapid (due to consumption) and is followed by a slow recovery if the underlying disease is adequately treated.

Classification of fetal and neonatal thrombocytopenia

- **Fetal** e.g. Alloimmune (NAIT), congenital infection, autoimmune (e.g. ITP, SLE), congenital/inherited (e.g. Wiskott-Aldrich)
- **Early onset** Fetal causes + placental insufficiency, perinatal asphyxia, infection, DIC, rare metabolic or inherited (e.g. TAR) syndromes
- **Late onset** Late onset sepsis, NEC, metabolic

Investigation

This depends on the clinical picture:

- **Maternal autoimmune** disease (ITP, SLE etc.) – cord platelet count
- **NAIT or suspected NAIT** (e.g. fetal intracranial haemorrhage) – cord platelet count, repeat after 2-4 hours if abnormal, discuss with neonatal and haematology consultant (see below)
- Signs of **sepsis** – FBC, cultures etc.
- Significant **bleeding** – check clotting as well
- ? **congenital infection** – look for jaundice, cataract, retinitis, organomegaly, lymphadenopathy – and consider the following *after receiving maternal assent*:
 - conjugated SBR/LFTs
 - urine CMV PCR
 - Toxoplasma IgG
 - Rubella and/or HIV depending on maternal details
 - Ophthalmology opinion
 - Cranial USS

Neonatal alloimmune thrombocytopenia (NAIT)

In the otherwise well term baby presenting with purpura or haemorrhage NAIT is the commonest cause of severe neonatal thrombocytopenia and should be assumed if maternal platelet counts are normal. **NAIT is potentially fatal and may require immediate intervention.**

NAIT is the platelet equivalent of haemolytic disease of the newborn and results when maternal antibodies to fetal platelets cross the placenta and cause platelet destruction.

The incidence is 1:1100 live births and during the first pregnancy in 40-50% of cases. The NBS Consultant on-call 0191 219 4400 and RVI Haematologist on-call should be contacted for advice. This will normally involve: take maternal blood (20mls EDTA, 10mls clotted), paternal blood (20mls EDTA) and infant blood (1ml EDTA) should be sent by taxi to National Blood Service, Holland Drive NE2 4NQ. This is currently then forwarded to Dr Lucas in Bristol (0117-9912110). Maternal HPA1a status (responsible for 80% of NAIT) is available within 24 hours (Monday-Friday), and full results by the next day. In up to 10% of cases, antibodies may only be detected on repeat testing.

Platelet counts may fall rapidly so if the first count is $<100 \times 10^9/l$ you may need to repeat a few hours later. If the initial count is $<50 \times 10^9/l$ urgent transfusion is indicated and the baby should be discussed with the consultant. Consider the need for a cranial ultrasound scan bearing in mind that this may miss small subdural bleeds.

There is evidence that transfusion at levels above $50 \times 10^9/l$ does not affect the incidence of haemorrhage. Below that level, it is unclear what constitutes a safe level, but bleeding or suspected NAIT should be transfused at a higher level than a baby who is well or where NAIT is not likely.

In possible NAIT, discuss with haematology, take blood for serology but do not await the result, transfuse if any suggestion of ICH or if platelet count $<50 \times 10^9/l$ with, in order of preference, depending on clinical status and availability:

1. HPA 1a 5b negative platelets ideally (suitable 95% NAIT; kept Sheffield, Bristol)
2. HPA 1a negative platelets (suitable 80% NAIT)
3. Random platelets with intravenous immunoglobulin 1g/kg/day for 2 days.

There is some evidence that IVIG can improve platelet counts in NAIT, although the rise may be delayed 12-36 hours and it can be used with random platelets if HPA negative platelets are unavailable. In some cases washed maternal platelets have been used.

Keep the platelet count above $50 \times 10^9/l$ for the first 2 weeks of life or until no further evidence of haemorrhage. Most cases should be normal by 2 weeks. In untreated cases ICH occurs in about 10% with long-term developmental sequelae in 20% of survivors.

Neonatal Autoimmune Thrombocytopenia

Transplacental passage of maternal platelet auto-antibodies (usually in the context of immune thrombocytopenic purpura or SLE) can cause neonatal thrombocytopenia, although this is usually much less problematic than in NAIT. Thrombocytopenia occurs in ~10% of babies whose mothers have these antibodies.

All babies born to mothers with these antibodies should have a cord/peripheral FBC done at birth. If platelets are normal then no further action is needed, but if $<150 \times 10^9/l$ this should be repeated at 2-3 days when counts are often at their lowest. Rarely thrombocytopenia can persist for weeks, and if it is severe then consideration should be given to IVIG treatment, to which most babies respond quickly.

References

1. Andrew M, Vegh P, Caco VC et al. A randomized, controlled trial of platelet transfusions in thrombocytopenic premature infants. *J Pediatr* 1993;**123**:285-91
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3. Roberts IAG, Murray NA. Thrombocytopaenia in the newborn. In Michelson A, ed. The platelets. New York:Elsevier Science, 2002:635-8
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5. Roberts I, Stanworth S, Murray NA. Thrombocytopenia in the Neonate. *Blood Reviews* 2008; **22**: 173-86