Neonatal Alloimmune Thrombocytopenia

University Hospitals of Leicester NHS Trust

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Contents

1. Introduction and Who Guideline applies to

This guideline is aimed at all Health care professionals involved in the care of infants within the Neonatal Service.

Key Points

- Fetal and Neonatal alloimmune thrombocytopenia (FNAIT) has a spectrum of disease ranging from subclinical moderate thrombocytopenia to catastrophic intracranial haemorrhage and death.
- Consider FNAIT in any infant with unexplained bleeding or thrombocytopenia (platelet count <100 $x10^9$/l.)
- If FNAIT suspected, use compatible platelets (usually HPA1a and 5b negative)
- Platelet transfusion thresholds are listed below

Background

- Fetal and Neonatal alloimmune thrombocytopenia (FNAIT) is a disorder caused by feto-maternal platelet incompatibility analogous to that in Rhesus Haemolytic Disease, with maternal anti-platelet antibodies crossing the placenta and destroying fetal platelets.
- The majority of cases are caused by antibodies directed against Human Platelet Antigen-1a (HPA-1a) and HPA-5b, but many rarer reactions have been reported.
- Prospective studies have shown incidence to be 1:1,100 live births, but the condition is under-reported.
- Mortality is around 10% of presenting cases, with neurological sequelae, including intracranial haemorrhage and subsequent neurodevelopmental delay in up to 25%.

2. Guideline Standards and Procedures

- Consider FNAIT in all cases of unexplained neonatal thrombocytopenia (Platelets <100 x 10^9/l).
- If FNAIT suspected, neonatal team should liaise with haematologists.
- Send maternal and paternal blood samples (via blood bank) to Bristol blood group reference lab for platelet antigen genotype and detection of maternal alloantibody to paternal platelets. (See Table 1)
- Sample request forms can be found at https://hospital.blood.co.uk/diagnostic-services/histocompatibility-and-immunogenetics/hi-test-request-forms/ Form 3D required (Platelet immunology

Table 1: Required tests and samples

	SAMPLES REQUIRED		TESTS
	EDTA (red topped tube) 	Clotted Serum (Gold/white topped tube)	
Maternal	6 mls	6 mls	Antibody screen vs Donor platelets Platelet HPA genotype Cross match maternal serum with paternal platelets
Paternal	6 mls	_	Cross match maternal serum with paternal platelets Platelet HPA genotype
Baby	1 ml	_	Platelet HPA genotype

- Monitor neonatal platelet count daily as it can continue to fall for the first 48 hours after birth.
- In suspected FNAIT if the platelet count falls below 50 x 10^9/l or if symptoms occur, perform a cranial ultrasound scan to exclude intracranial haemorrhage

Platelet count thresholds for neonatal platelet transfusion*:

- **For the asymptomatic baby**

Transfuse compatible platelets (usually HPA1a and 5b negative), even if there is no active bleeding and no family history of intracranial haemorrhage. There are two important points to consider here regarding what threshold to use

1. The national recommended standard for transfusion of platelets where FNAIT is confirmed or highly likely, is <30 $x10^9$/l.

2. Where FNAIT is not a diagnosis or is not a likely differential diagnosis, the neonatal recommended threshold to transfuse such babies, is <25 x 10^9/l [see Estcourt et al PLANET 2 study, New et al and BCSH guideline 2016, addendum 21.08.2020]).

Use a cut off of Platelet count <25 x109/L to initially transfuse.

(This is to facilitate streamlining, uniformity of practice, and also based on the relative unlikelihood of FNAIT vs non FNAIT diagnoses. Once a diagnosis of FNAIT is confirmed, the threshold can change to 30 x 109/L for need for further transfusions)

- **For neonates with bleeding**, current coagulopathy, before surgery, or infants with FNAIT if previously affected sibling with intracranial haemorrhage

Use a cut off of Platelet count <50 $x10^9$/l to transfuse

- **For neonates with major bleeding or requiring major surgery** (e.g. neurosurgery)

Use a cut off of Platelet count <100 $x10^9$/l to transfuse

On-going monitoring/management

- In the presence of life threatening bleeding (such as intracranial or gastrointestinal bleeding), platelets should be transfused to maintain platelet count >100 $x10^9$/l initially then >50$x10^9$/l for at least 7 days

- A neonate with FNAIT should have platelet counts monitored until there is no further clinical evidence of platelet consumption.

- If FNAIT is suspected and platelet transfusion is required, DO NOT wait for results of confirmatory tests before transfusing platelets.

- HPA1a and 5b negative donor platelets should be used if promptly available. This will require authorisation from NHSBT on call (haematology registrar to coordinate). If HPA-selected platelets are not immediately available, HPA unselected platelets should be transfused if a platelet transfusion is indicated.

- In the very rare event of HPA selected or HPA non selected platelets being unavailable, give IV immunoglobulin (1g/kg/day for 1-3 days). Any effect on platelet count will be delayed for 24-72 hours. Where used, parent(s) should be provided with information and their verbal consent obtained.

- Notes: See the Trust link at Immunoglobulins | Pharmacy and Medicines - UHL Connect (uhl-tr.nhs.uk) Although 1g/kg/day can be given for three doses, recent

immunology commissioning guidelines note that after 2 doses of 1g/kg/day in FNAIT, panel approval will be required if a third dose is needed.

- If there is little or no increment following HPA matched platelet transfusion, give IV immunoglobulin (1g/kg/day for 1-3 days). Any effect on platelet count will be delayed for 24-72 hours. IV immunoglobulin should not be used as sole treatment for a neonate with bleeding or severe thrombocytopenia. Where used, parent(s) should be provided with information and their verbal consent obtained.

For added information on antenatal counselling, see Appendix 1.

3. Education and Training

None

4. Audit standards

If platelets <30x10^9/l, documentation of platelet transfusion or reason for deferring (100%).
HPA1a and 5b negative donor platelets should be used (100%).
Document in front of the maternal notes about potential risks (100%)

5. Supporting References

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6. Key Words

Bleeding, Haemorrhage, Platelets, Transfusion

The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

Contact and review details			
Guideline Lead (Name and Title) A Webster – Consultant Haematologist H Qureshi – Consultant Haematology and Transfusion T Pillay – Consultant - Neonatal S Mittal – Consultant & guideline lead			**Executive Lead** Chief Medical Officer
Details of Changes made during review:			
Date	**Issue Number**	**Reviewed By**	**Description Of Changes (If Any)**
1999	**1**	**New document**	Authors: Dr S Pavord & Dr C Hawork
2005	**2**	Dr S Pavord & D Elliott,	Updated
March 2011	**3**	Dr S Pavord, P Coser & M Copple	Updated
July 2013	**4**	N Rafeullah, A Grover, S Pavord	Neonatal unit update:
July 2018	**5**	Neonatal Guidelines Meeting	
October 2021	**6**	August 2021; Haematology and Neonatal update September 2021; Neonatal Guidelines meeting Neonatal Governance Meeting	Added Fetal to Fetal and Neonatal alloimmune thrombocytopenia (FNAIT) Sample request forms sign post added Platelet count thresholds for neonatal platelet transfusion guidance updated including specification for treating asymptomatic, bleeding and major bleeding infants. On-going & monitoring guidance updated.
January 2025	**7**	Neonatal Guidelines Neonatal Governance	Updated tests and samples table

Appendix 1: Supportive Information

Antenatal counselling and management:

- The mother should receive counselling about the risks for, and management of, subsequent pregnancies (75-90% will be affected)
- She should be informed of risks associated with blood transfusion (Post-transfusion purpura). Risk now minimal with use of leukodepleted blood.
- Arrange pre-pregnancy counselling for any subsequent pregnancy
- Offer National Blood Service leaflet 'Platelet groups & Antibodies in Pregnancy'
- Document on front of all sets of maternal patient notes:

Warning: Patient has potential risk of fatal complications after blood transfusion
And, in addition on the front of maternity notes:
Warning: Fetus at risk of alloimmune thrombocytopenia.

- Sisters of women with FNAIT with child bearing potential should be screened as they at potentially increased risk. They should be referred to haematology for this to be arranged.

Subsequent pregnancies

- Early booking appointment. Fast tracked/ self-referral if possible.
- Engage with haematologist and fetal medicine team early
- Discuss risks to fetus (pre-pregnancy counselling)
- Determine whether the father is homozygous or heterozygous for the relevant antigen. If heterozygous do fetal platelet genotyping.
- Outline antenatal care plan.
- USS to determine gestation.
- Steroids and IV Immunoglobulin should be given from 12 weeks if history of fetal haemorrhage in previous pregnancy, otherwise from 20 weeks.
- Refer to specialist centre for fetal blood sampling at 20-24 weeks if there was a haemorrhage in the previous fetus, otherise refer at 28 weeks. Further management by intrauterine transfusions if necessary should be done at the specialist centre.
- The timing of further fetal blood sampling and transfusion procedures depends on the platelet count at the initial fetal blood sampling.
- IV immunoglobulin may need to be doubled or discontinued depending on whether there has been partial or no response respectively.
- Delivery should be by elective caesarean section with compatible platelets available (alternatively intrauterine platelet transfusion followed by vaginal delivery to be done at specialist centre)
- Check cord platelet count. if $<30 \times 10^9$/l/ symptomatic, treat as above.

Screening

- Previous or family history of FNAIT
- Also consider screening for mothers of neonates with unexplained thrombocytopenia, hydrocephalus or unexplained late fetal loss particularly where there has been an intracranial haemorrhage.