LOCAL OPERATING PROCEDURE

NEONATAL SERVICES DIVISION

Approved by Neonatal Services Quality Committee
April 2018

NEONATAL ALLOIMMUNE THROMBOCYTOPENIA (NAIT)

This LOP is developed to guide safe clinical practice in Newborn Care Centre (NCC) at The Royal Hospital for Women. Individual patient circumstances may mean that practice diverges from this Local Operations Procedure (LOP).
This LOP has been developed in partnership with the Haematology team at Sydney Children's Hospital and the Australian Red Cross. Using this document outside the Royal Hospital for Women or its reproduction in whole or part, is subject to acknowledgement that it is the property of NCC and is valid and applicable for use at the time of publication. NCC is not responsible for consequences that may develop from the use of this document outside NCC.

INTRODUCTION

Neonatal alloimmune thrombocytopenia or "NAIT" or fetomaternal alloimmune thrombocytopenia (FNAIT) is a rare but serious condition. It is associated with significant neonatal morbidity and mortality, including a 20% risk of intracranial haemorrhage (ICH). Platelet antigens, inherited from the father and expressed on neonatal platelets, are destroyed by maternal alloantibodies, which cross into the neonatal circulation via transplacental transfer. Immediate management includes confirmation of diagnosis, use of specific platelets (mostly HPA-1bb) to keep the platelet count above 30 x 10^9/L and immune-modulatory treatment. There are risks to subsequent offspring, which are higher if the first offspring with identified NAIT experienced an ICH.

1. AIM

- To identify potential cases of NAIT
- To assist in immediate clinical management of the neonates affected with NAIT
- To arrange appropriate follow up

2. PATIENT

- Newborns

3. STAFF

- Medical and nursing staff

CLINICAL PRACTICE

When to suspect NAIT:

- Severe thrombocytopenia in an otherwise well neonate even if no history of NAIT in previous pregnancies (< 50 x 10^9/L) although NAIT can occur with mild/moderate thrombocytopenia (< 150 x 10^9/L)
- Exclude alternative diagnoses, such as infection, collection error, maternal auto-antibodies (especially maternal ITP), maternal medications, neonatal liver disease
- NAIT in a prior pregnancy (although NAIT can occur in the first pregnancy)

Diagnosis and immediate management:

- Arrange neonatal full blood count if thrombocytopenia is suspected on history or clinical examination
- If the diagnosis is suspected, treat as NAIT (confirmatory tests may take a few days)
- Contact Paediatric Haematology Fellow/Consultant
- Call Australian Red Cross Blood Service (ARCBS) – 1300 478 348
    - 24 hour phone line, request the Medical Officer on call
    - Request rare platelets type HPA-1bb, unless prior platelet genotyping on the parents is available to suggest use of another HPA (human platelet antigen) group
    - Transfuse to keep neonatal platelet count above 30, preferably above 50 x 10^9/L
    - Rare platelets will always be available from ARCBS (usually HPA-1bb platelets)
    - Rare HPA-1bb platelets are also genotyped for other HPA types
    - It may be possible to provide another HPA-type if the HPA antibody is known

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- Urgently collect blood from both parents and the baby
    - Samples required are indicated on the ARCBS cover page for requests (see appendix A) or can be downloaded from the ARCBS website www.transfusion.com.au
        - Mother – 10ml clot tube (no gel) and 20ml EDTA tube, Father – 20ml whole blood EDTA tube only, Baby – 1-2ml EDTA tube
    - The form is available below (see appendix B) or can be downloaded from the ARCBS website www.transfusion.com.au
    - Please use a form for each parent and indicate in "Tests Required Section" that NAIT testing is needed
        - Fresh samples (collected within the last 24 hours) must be delivered, transported at ambient temperature, to ARCBS within working hours Monday to Friday (testing will not occur on a weekend)
    - Advise SEALS Blood Bank and ARCBS about urgency and transport of samples
    - Blood can be couriered to ARCBS, to arrive as early as possible. Preliminary results will be available on the same day if samples arrive by mid-morning
- If preliminary results are positive (for example if maternal serum alloantibodies to HPA-1a are present) then the neonate needs URGENT TREATMENT to reduce the risk of ICH
- Solid Phase platelet (intact platelet panels) antibody investigations and HPA genotyping are performed urgently and results sent out as a preliminary result, which is followed up with definitive MAIPA assays (Monoclonal Antibody-specific Immobilisation of Platelet Antigens assay)
- MAIPA assays have been developed to allow identification and characterisation of antibodies directed against platelets (with platelet glycoproteins)
- Arrange head ultrasound to exclude ICH (further imaging may be required)
    - This should be performed as soon as possible as infants are at high risk of ICH
    - A suspected antenatal ICH may have implications for subsequent pregnancies

Treatment:
It is important to maintain platelet counts above 30 x 10^9/L and preferably above 50 x 10^9/L

- Platelet transfusions are the mainstay of initial therapy, followed by Intravenous immunoglobulin (IVIG) and possibly steroids (platelets are ideally CMV negative and irradiated – if CMV negative platelets are not available, then discuss with the haematologist)
- Volumes advised are 10-20ml/kg
- HPA antigen negative platelets are preferred, but random donor platelets (HPA antigen positive) can also be used safely and effectively if HPA antigen negative platelets are not available
- Repeat testing for platelet level is required (for neonates with severe NAIT, a one-hour post-platelet increment may be useful)
- Please advise ARCBS of the neonate's clinical status and likely need for further rare platelets
- Maternal platelet collection is also a possibility however this procedure is rarely performed (please speak to Blood Bank and ARCBS)
- In addition to platelet transfusion, treatment with IVIG is strongly recommended – the dose is 1g/kg x 2 days (ordered from ARCBS and administered intravenously)
- Consider addition of steroids for severe/ refractory NAIT (suggested dose: IV methylprednisone 1-2mg/kg/ day in 2-3 divided doses x 5 days)
- Seek further advice from Haematology in severe/refractory NAIT cases
- Treatment side effects to be discussed with the parents include (but are not limited to):
    - IVIG – allergic/anaphylactic reactions, fever, headache, aseptic meningitis (rare)
    - Steroids – hypertension (that may require additional treatment), hyperglycaemia, irritability, mood changes, avascular necrosis, transient adrenal suppression

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Follow up:

- As NAIT is purely a consequence of maternal antibodies directed against paternal platelet antigens NAIT will resolve after 1-3 weeks
- Monitoring of platelet counts for at least 2-6 weeks post delivery is recommended
- Consider reporting the case to the Australian NAIT registry to inform epidemiological studies
- Arrange haematology follow-up as an outpatient
- Arrange referral for parents to a maternal foetal medicine specialist for follow up
- Advise parents that subsequent pregnancies are at risk and early antenatal, or preferably pre-conception, counselling with a maternal foetal medicine subspecialist is recommended

4. EDUCATIONAL NOTES

Epidemiology:

- NAIT accounts for 3% of all fetal and neonatal thrombocytopenia (defined as platelets < 150 x 109/L) and 27% of severe cases (platelets < 50 x 109/L)
- NAIT is associated with significant neonatal morbidity and mortality, including a 20% risk of intracranial haemorrhage (ICH)
- NAIT can occur in the first pregnancy

Risk factors:

- NAIT in a prior pregnancy is a risk factor for NAIT in subsequent pregnancies, especially where there is known discordance between parental HPA (human platelet antigen) types (see table below)
- HPA types vary in frequency across racial groups. The most frequent cause of NAIT in a Caucasian population is anti-HPA-1a antibodies and in Asian populations are anti-HPA-4a antibodies
- Other HPA antibodies implicated in NAIT include anti-HPA-3a, anti-HPA-5b, anti-HPA-15a and anti-HPA-15b
- Severe NAIT and ICH in a prior pregnancy greatly increases the risk of ICH in subsequent pregnancies

Future pregnancies:

- Through NAIT testing, parental HPA typing is determined and the risk to future pregnancies can be predicted (see table below)
- In-utero HPA genotyping can be performed on DNA extracted from amniocytes (DNA extraction, and confirmatory testing that DNA is of foetal origin, is performed by the Molecular Genetics Unit at Prince of Wales Hospital) –the DNA is then referred to the Tissue Typing Department at the ARCBS for HPA-genotyping
- Amniocytes should also be cultured in the cytogenetic laboratory to allow for subsequent retesting if needed
- If NAIT is considered likely either from history and/or prenatal invasive diagnosis, antenatal therapy may be instituted (this may include IVIG and/or steroids and possible in-utero platelet transfusion)
- Treatment depends on the previous history of severity of thrombocytopenia, including any history of previous ICH
- ARCBS can be contacted peri-partum to ensure availability of specific platelets. A follow-up antibody screen post-partum is often useful, to confirm genotyping and determine if additional HPA antibodies have developed

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Causative Maternal HPA allo-antibody	Maternal HPA type	Paternal HPA type	Offspring HPA type	Platelets required for transfusion
Anti-HPA-1a antibody These maternal antibodies are directed against HPA-1a antigens expressed on the neonatal platelets	HPA-1bb	HPA-1aa *or* HPA-1ab	If father HPA-1aa, then 100% of offspring are HPA-1ab, therefore 100% affected If father HPA-1ab, then 50% of offspring affected (HPA-1ab) Offspring who are HPA-1bb will be unaffected	HPA-1bb These are negative for HPA-1a antigens, to which the maternal alloantibodies are directed

5. RELATED POLICIES/PROCEDURES/CLINICAL PRACTICE LOP

- Platelet Transfusion

6. RISK RATING

- Medium

7. NATIONAL STANDARD

- Standard 1 Governance for Safety and quality in Health Service Organisation
- Standard 11 Service Delivery
- Standard 12 Provision of Care

8. ABBREVIATIONS AND DEFINITIONS OF TERMS

NAIT	Neonatal Alloimmune Thrombocytopenia	ARCBS	Australian Red Cross Blood Service
NCC	Newborn Care Centre	HPA	Human Platelet Antigen
LOP	Local Operations Procedure	MAIPA	Monoclonal Antibody-specific Immobilisation of Platelet Antigens
FNAIT	Fetomaternal Alloimmune Thrombocytopenia	IVIG	Intravenous immunoglobulin
ICH	Intracranial Haemorrhage		

9. REFERENCES

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2. McQuilten Z, Wood EM, Savoia H et al. A review of pathophysiology and current treatment for neonatal alloimmune thrombocytopenia (NAIT) and introducing the Australian NAIT registry. Australian and New Zealand Journal of Obstetrics and Gynaecology. 2011;51:191-198
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10. AUTHORS

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Revised	5/4/2018	NCC LOPS Committee

REVISION & APPROVAL HISTORY
Reviewed April 2018
Aproved Newborn Quality Committee 4/2/13

FOR REVIEW :

…../Appendices

APPENDIX A: Parental blood sample information

NEW SOUTH WALES TRANSPLANTATION AND IMMUNOGENETICS

Australian Red Cross BLOOD SERVICE

Sample Delivery (24 hours)
Dock A, Level 3 17 O'Riordan Street
Alexandria NSW 2015

ASHI accreditation: 02-9-AU-01-1
NATA accreditation: 18808

Enquiries
8:00am to 4:30pm
+61 2 9234 2322 (phone)
+61 2 9234 2326 (fax)

DL-NSWTTCBO@redcrossblood.org.au
www.transplantservices.com.au

Sample and Volume Requirements

REQUEST FORM:

Request forms and sample labels must be completed accurately and have legible handwriting. Alternatively, the request form can be filled out online or a hospital label can be used.

Information on the form must match that on the sample tube(s).

Ensure that all tubes, at a minimum, are clearly labelled with:

- The patients full name (family name and given names),
- Date of birth
- And date of collection, as indicated on the request form.

Ensure the request form contains a minimum of three forms of unique identifiers (for example: full name, date of birth, MRN, Medicare number)

If these are not provided, testing may be delayed.

DELIVERIES:

Samples should be sent to: **Transplantation & Immunogenetics Services – NSW**
Australian Red Cross Blood Service
Dock A – Blood Inwards
17 O'Riordan Street
ALEXANDRIA NSW 2015

SPECIMENS:

Samples (other than frozen samples) should be maintained at room temperature.

The quality of typing cannot be guaranteed for samples that are not received at room temperature or not received within 24 hours of collection.

Samples sent for crossmatching prior to living renal transplantation must be pre-booked. Please email ttcbo@redcrossblood.org.au

SOLID ORGAN TRANSPLANTATION

Testing	Request	Specimen	Volume	Collection
Recipient entry- NSW/ACT waiting list *Activation form requested	TWL- entry	Whole blood	30 mL	ACD tubes
		clot	10mL	With gel
Monthly serum sample for solid organ crossmatch trays (not required for Liver transplantation)	Monthly	clot	10mL	With gel

For paediatric volumes please call the lab on (02) 9234 2351

PLATELET IMMUNOLOGY

Testing	Sample Details	Volume	Collection
Fetomaternal Alloimmune Thrombocytopenia (FNAIT	Mother	10 mL	Clot – no gel
		20mL	EDTA tubes
	Father	20mL	EDTA tubes
	Baby	1-2 mL	EDTA tubes
Platelet autoantibodies, Post Transfusion Purpura, Platelet Function Disorder	Clot	10 mL	Clot – no gel
	Patient platelet count >20x10^9/L	30 mL	EDTA tubes
	Patient platelet count >50x10^9/L	20 mL	EDTA tubes

LIVE DONOR KIDNEY WORKUPS

Testing	Request	Specimen	Volume	Collection
Recipient	Stages 1, 2 and 3	Whole Blood	40 mL	ACD tubes
		Clot	10 mL	With gel
Live Donor	Stages 1, 2 and 3	Whole Blood	40 mL	ACD tubes

BONE MARROW TRANSPLANTATION

Testing	Request	Specimen	Volume	Collection
Initial patient testing	Initial	Whole Blood	20 mL	ACD tubes
Related donor testing	Family members	Whole Blood	20 mL	ACD tubes
Verification patient testing	VT	Whole Blood	20 mL	ACD tubes
		Clot	10 mL	With gel
Verification related donor testing	VT	Whole Blood	20 mL	ACD tubes
		Clot	10 mL	With gel
Refractoriness to Platelet Transfusion		Clot	10 mL	Clot – no gel
		Patient WBC ct >1x10^9/L	20 mL	ACD
		Patient WBC ct <1x10^9/L	40 mL	ACD

Paediatrics patients/donors: Initial and verification testing – 1ml/ACD/birth year up to 8yo, (+ 0.5 mL serum for patients at VT).

APPENDIX B: Parental sample request form

NEW SOUTH WALES TRANSPLANTATION AND IMMUNOGENETICS

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RCPA NATA ASHI

Enquiries
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Sample Delivery (24 hours)
Dock A, Level 3 17 O'Riordan Street
Alexandria NSW 2015

ASHI accreditation: 02-9-AU-01-1
NATA accreditation: 18808

treportingnsw@redcrossblood.org.au
www.transplantservices.com.au

Platelet Investigation Request Form

Urgent results: Please contact the laboratory on the above phone number or email address

LABORATORY USE ONLY	
SPECIMEN ID	DATE AND TIME STAMP

PATIENT DETAILS	**Please fill or affix hospital label here – three forms of ID required**
SURNAME (Please print)	DOB
GIVEN NAMES	☐ MRN ☐ MEDICARE No. (Please complete)
ADDRESS	
	☐ FEMALE ☐ MALE
FNAIT ONLY: NAME AND DOB OF PARTNER/BABY (A **separate** request form is required)	☐ MOTHER ☐ FATHER ☐ BABY
DIAGNOSIS/CLINICAL NOTES	
REFERRED BY	CONTACT NUMBER

REPORT TO	**COPY OF REPORT TO**
NAME	NAME
ADDRESS	ADDRESS
EMAIL	EMAIL

TESTING REQUIREMENTS	**Refer to website regarding sample volume for paediatric patients or patients with low cell counts**	
☐ PLATELET REFRACTORINESS (20mL ACD + 10mL CLOT)	☐ PRE-TRANSPLANT SAMPLES	☐ POST-TRANSPLANT SAMPLES
(A request for **HLA-HPA compatible platelets / clinical information** form must be filled out and forwarded to: Transfusion Medical Services, contact 9234 2265)		
☐ FNAIT INVESTIGATION (Mother: 20mL EDTA + 10mL CLOT; Father: 20mL EDTA; Baby: 1–2mL EDTA)		
(Individual request forms are required for **each family member**)		
☐ PLATELET FUNCTION DISORDER (20mL EDTA + 10mL CLOT)	☐ TRALI INVESTIGATION (20mL EDTA + 10mL CLOT)	
☐ PTP INVESTIGATION (20mL EDTA + 10mL CLOT)	☐ OTHER (Specify)	

SAMPLE COLLECTION	**Recommended transportation: Whole blood samples: Room temperature. Separated serum samples : <4°C. Samples should be received by laboratory within 24 hours of collection. Ensure samples are packed in a secure container and the outside of the transport container is clearly labelled with the delivery address.**		**COMPLETED BY COLLECTOR**
COLLECTOR NAME	DATE AND TIME OF COLLECTION	ACCESSION No.	
PATIENT SIGNATURE (Confirming samples are labelled correctly)	DATE		
SAMPLE TYPE: ☐ WHOLE BLOOD (ACD) ☐ CLOTTED ☐ OTHER (Specify)			

PRACTITIONER/DELEGATE SIGNATURE	**DATE OF REQUEST**

FRM-01678 Version: 1 Date effective: 23/10/2017