INITIAL MANAGEMENT OF SUSPECTED NEONATAL ALLOIMMUNE THROMBOCYTOPENIA

☐ Well baby with a repeated platelet count ≤ 80x10⁹/L, who is not dysmorphic, usually AGA, with history & exam not suggestive of TORCH, and mother with normal platelet count & no history of ITP

☐ Send maternal blood for testing of NAIT to CBS, consult hematology through neonatology, and arrange for a day-3 head US

☐ Platelet count 50-80x10⁹/L
  ☐ Repeat platelet count q12h until >80x10⁹/L, then q24h until >150x10⁹/L
  ☐ If platelet count drops <50x10⁹/L, go back to top

☐ Platelet count 30-50x10⁹/L
  ☐ Repeat platelet count q6h until >50x10⁹/L
  ☐ If platelet count drops <30x10⁹/L, go back to top

☐ Platelet count <30x10⁹/L
  ☐ Notify Transfusion medicine Laboratory (TML)*
  ☐ Administer 1g/kg IVIG followed by 15mL/kg of random donor platelets ASAP. Give 2d dose of IVIG 24h after the 1st dose
  ☐ Repeat platelet count 1 hour after transfusion

☐ Active bleeding (intracranial, GI, etc)
  ☐ Do PT/INR, aPTT, fibrinogen, D-dimer, and coagulopathy, and give 15mL/kg of random donor platelets ASAP

☐ Manage coagulopathy if screen abnormal

☐ Platelet count <30x10⁹/L, or active bleeding
  ☐ Repeat random donor platelet transfusion
  ☐ Through TML request allogeneic HPA-1 negative platelets from CBS; if the product will not be available in < 6 hours, request that TML organize apheresis maternal platelets (plasma reduced) if maternal condition permits
FAQ:

When should platelet transfusions be considered in newborns?

The only evidence-based recommendation is based on Andrew's RCT: no benefit (reduction in significant hemorrhage) when platelet transfusions were administered for platelet count in the range of 50-100x10^9/L. Did not establish lower limit of platelet count below which the risk of hemorrhage increases.

In stable NICU babies, all guidelines recommend transfusion when platelet count falls below 20-30x10^9/L.

In unstable NICU babies, many recommend transfusion when the platelet count is in the range of 30-50x10^9/L.
- ELBW < 1000g in the first week of life
- Babies receiving intensive care (e.g. ventilation) with fluctuating vital signs, specially BP and perfusion
- Previous recent significant bleeding (e.g. IVH or pulmonary hemorrhage)
- Currently bleeding (petechiae, oozing, bruising) or with coagulopathy

Some recommend that babies with active bleeding (pulmonary hemorrhage or ICH) be transfused to platelet count > 100x10^9/L.

When is a transfusion successful?

As the only evidence-based safe level is ≥ 50x10^9/L, platelet transfusions should aim at exceeding this level.

All platelet transfusions should be followed with a platelet count 1 hour post-transfusion, to guide the timing of subsequent transfusions and suggest the mechanism of thrombocytopenia (consumption vs decreased production)
How is the response to random platelet transfusion supportive or not of NAIT?

In Caucasians, the absence of response to a random platelet transfusion is strong presumptive evidence of NAIT, as 98% of caucasian donors are HPA-1a positive, and their platelets are, therefore, incompatible in this clinical situation.

A good response to a random platelet transfusion is more likely in cases due to alloantibodies other than HPA-1a. For example, random platelet transfusion would be effective in approximately 80% of HPA-5b alloantibodies.

How is IVIG requested from Transfusion Medicine Laboratory (TML)?

IVIG can be made immediately available upon request, and explanation of need and urgency.

Effectiveness of IVIG:

IVIG is not as effective in severe NAIT as in ITP, and it is not as rapidly effective as compatible platelets. However, compatible platelets are usually not as readily available as IVIG.

IVIG has been shown to improve the platelets increment and duration of response following transfusion of random donor platelets to patients with ITP. Limited experience suggests that this is also the case in NAIT.

Indications for second dose of IVIG

The most commonly recommended regimen is of 1g/Kg on 2 consecutive days.

What is the most effective therapy for babies with severe NAIT?

A platelet count >50x10^9/L is achieved faster by transfusing with HPA compatible platelets (donor or washed maternal), however neither product is immediately available.

IVIG is effective in raising the platelet count although the rise may be delayed for 24-48 hours. IVIG may be combined with random donor platelet transfusion and this combination may achieve a transient rise in platelet count until IVIG becomes effective. This approach is used in most cases with marked thrombocytopenia as antigen-negative platelets are usually not immediately available.

Treatment with HPA-1a negative platelets, or with IVIG-random platelet combination is more desirable than with maternal platelets, unless timely and thorough testing for blood-transmissible disease is available.

When HPA status is unknown, transfusion with donor platelets which are HPA-1 negative will be effective in the vast majority of cases.

How is the process to obtain IVIG and compatible platelets initiated?

The process needed to obtain compatible platelets starts with a phone call to the TML, who will contact the hematopathologist on call. This call should be made as soon as a patient with NAIT is suspected.

IVIG and random platelets will be released if immediate treatment is needed. If criteria are met, these products will be released to go out with the transport team so that treatment can be initiated at the referring center.
INITIAL MANAGEMENT OF SUSPECTED NEONATAL ALLOIMMUNE THROMBOCYTOPENIA

The TML staff will then initiate the search for HPA-1a negative platelets, from registered donors and/or product in Vancouver, Calgary and Winnipeg. The timeframe for their availability on site will be determined.

A platelet count will be done after the IVIG and random platelet transfusion has been completed. The results will determine if additional transfusions, including with HPA negative platelets are needed.

When should maternal NAIT testing be initiated?

As soon as possible, maternal blood should be sent to the Canadian Blood Service for NAIT testing. Blood-transmissible disease testing is sent to the BC CDC.

When will maternal platelets be provided for the treatment of severe thrombocytopenia in NAIT?

Apheresis of maternal platelets will only be provided when it is urgently needed and HPA platelets cannot be obtained in a reasonable timeframe (6-12 hours).

Due to constraints on the availability of timely and thorough testing for blood-transmissible disease, treatment with maternal washed platelets is less desirable than with HPA compatible platelets, or with IVIG-random platelet combination.

How long does NAIT related thrombocytopenia last?

While initial thrombocytopenia is usually severe, 75% of affected newborns recover normal platelet counts by 10 days of age. However, complete spontaneous recovery may be delayed for up to 12 weeks.

What is the chance that the platelet count will drop again?

The half life of IgG is approximately 21 days. Most infants with NAIT recover normal platelet counts by 10 days of age, but others may be thrombocytopenic as long as 12 weeks.

We recommend that once an infant is in the recovery period (platelets >100x10^6/L, platelet count should be monitored weekly until >150x10^6/L

Is there a role for steroids in the management of NAIT?

IVIG and plasma-reduced maternal platelets or allogenic HPA-1a negative platelets are the mainstay treatment in NAIT. Steroids have been used in NAIT but there is no convincing evidence that they are effective.

The only circumstances where steroids might be considered are for babies with platelet count < 30x10^9/L when:

1) transport is not immediately available or will take more than 4 hours, and there is no IVIG available at the site, and there is no response to random platelets, (the three conditions must be met), or when

2) transport is not immediately available or will take more than 4 hours, and there is no IVIG available at the site, and there are no random platelets available (the three conditions must be met).

What are the most severe complications in NAIT?

Fetal or neonatal intracranial hemorrhage may be fatal or lead to long-term neurodevelopmental sequelae
in approximately 20% of survivors.

Should these children be imaged?

Evidence of intracranial hemorrhage has been documented in NAIT as early as the 16th week gestation. The most common site of bleeding is probably under the cerebral cortex, often within the temporal lobe. This may lead to subarachnoid and intraventricular bleed, posthemorrhagic hydrocephalus and porencephaly. According to one study, the risk of intracranial hemorrhage is 7% if a previously affected sibling did not have ICH, and 48% if a previously affected sibling did have ICH.

There is no established platelet threshold to determine who should be imaged. Therefore all infants with NAIT should be imaged at three days of age (consistent with other screening ultrasound recommendations). Subsequent to an abnormal screening ultrasound, it may be decided to perform a CT or MRI scan.

Does NAIT ever occur in a first pregnancy?

NAIT occurs during the first pregnancy in 40-50% of cases, and is therefore unpredictable.

How do we test for NAIT and other conditions with anti-platelet antibodies:

Name of the test:
Tests for maternal platelet antibodies

Samples:
- Blood testing in the mother:
  Obtain at least 5mls of clotted blood (red top), and at least 28mls of EDTA blood (mauve top). If the mother's platelet count is less than 100 x10^9/L a larger sample will be needed (45 mL)

Is subsequent testing needed in both parents?
Parents should be referred to an adult hematologist for further work-up related to future pregnancies (heterozygosity).

Additional reading:

3) Kaplan C. Immune thrombocytopenia in the foetus and the newborn: diagnosis and therapy. Transfus Clin Biol 2001;8:311-4