THROMBOCYTOPENIA

DEFINITION
• Platelet count <150 x 10^9/L
• mild (platelet count 100–150 x 10^9/L) and moderate (50–100 x 10^9/L) thrombocytopenia occur frequently in preterm infants who are ill, and in those born to women with pregnancy-induced hypertension (PIH)
• severe thrombocytopenia (<50 x 10^9/L) is uncommon, particularly in apparently healthy term infants and should raise possibility of neonatal allo-immune thrombocytopenia (NAIT; see below)

CAUSES

<table>
<thead>
<tr>
<th></th>
<th>WELL</th>
<th>ILL</th>
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</thead>
<tbody>
<tr>
<td>Term</td>
<td>Preterm</td>
<td></td>
</tr>
<tr>
<td>Common</td>
<td>• NAIT</td>
<td>• IUGR</td>
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<td></td>
<td>• IUGR</td>
<td>• Congenital infections</td>
</tr>
<tr>
<td></td>
<td>• Maternal diabetes</td>
<td>• Infection</td>
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<td></td>
<td>• Maternal ITP</td>
<td>• NEC</td>
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<tr>
<td></td>
<td>• Trisomies (13, 18, 21)</td>
<td>• Disseminated intravascular coagulation</td>
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<tr>
<td></td>
<td>• IUGR</td>
<td>• Perinatal asphyxia</td>
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<tr>
<td></td>
<td>• Congenital infections</td>
<td>• Congenital infections</td>
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<tr>
<td></td>
<td>• Thrombocytopenia Absent Radii (TAR) syndrome</td>
<td>• Thrombosis (renal, aortic)</td>
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<tr>
<td>Rare</td>
<td>• Congenital amegakaryocytic thrombocytopenia (CAMT)</td>
<td>• Congenital leukaemia</td>
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</table>

Severe thrombocytopenia in an otherwise healthy term newborn infant is NAIT until proved otherwise

INVESTIGATIONS
• Evaluation of early-onset (<72 hr after birth) thrombocytopenia (see Flowchart)
• in preterm infants with early-onset mild-to-moderate thrombocytopenia in whom there is good evidence of placental insufficiency, further investigations are not warranted unless platelet count does not recover within 10–14 days
• in preterm infants without placental insufficiency, investigate first for sepsis
• In term infants, investigate for sepsis and NAIT (see below)

Evaluation of late onset thrombocytopenia
• Thrombocytopenia presenting in neonate after first 3 days of life, presume underlying sepsis or necrotising enterocolitis (NEC) until proved otherwise
• these infants are at significant risk of haemorrhage, though the benefit of platelet transfusion is not clear-cut
**MANAGEMENT**

**General**

**Avoid**
- Heel prick, use venepuncture
- Invasive procedures
- Intramuscular injections
- Lumbar puncture
- If any of above are unavoidable:
  - discuss with on-call consultant
  - consider use of platelet transfusion before undertaking unavoidable invasive procedures
  - give particular attention to haemostasis
Platelet transfusion
- This is the only available immediate and specific therapy for thrombocytopenia but carries a risk of transfusion-related infections and transfusion reactions
- The following guidance is based on expert opinions and consensus statements

<table>
<thead>
<tr>
<th>Platelet count (× 10^9/L)</th>
<th>Non-bleeding neonate</th>
<th>Bleeding</th>
<th>NAIT (proven/suspected)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;30</td>
<td>Consider transfusion in all cases</td>
<td>Transfuse</td>
<td>Transfuse [with human platelet antigen (HPA) compatible platelets]</td>
</tr>
<tr>
<td>30–49</td>
<td>Do not transfuse if clinically stable</td>
<td>Transfuse</td>
<td>Transfuse if any bleeding (with HPA compatible platelets)</td>
</tr>
<tr>
<td></td>
<td>Consider transfusion if:</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>• &lt;1 kg and &lt;1 week old</td>
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<td></td>
<td>• clinically unstable (e.g. fluctuating blood pressure or perfusion)</td>
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<tr>
<td></td>
<td>• previous major bleeding</td>
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<tr>
<td></td>
<td>• (e.g. grade 3–4 IVH or pulmonary haemorrhage)</td>
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<tr>
<td></td>
<td>• current minor bleeding (e.g. petechiae, puncture site oozing or bloodstained ET secretions)</td>
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<td></td>
<td>• concurrent coagulopathy</td>
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<td></td>
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<tr>
<td></td>
<td>• requires surgery or exchange transfusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>50–99</td>
<td>Do not transfuse</td>
<td>Transfuse</td>
<td>Transfuse if any major bleeding (with HPA-compatible platelets)</td>
</tr>
<tr>
<td>&gt;99</td>
<td>Do not transfuse</td>
<td>Do not transfuse</td>
<td>Do not transfuse</td>
</tr>
</tbody>
</table>

Type of platelets
- NAIT: HPA compatible platelets wherever possible
- All others: blood group-compatible cytomegalovirus (CMV) negative
- Irradiation of platelets is not routinely required but should be considered for infants with definite or suspected immunodeficiency or those who have undergone intrauterine transfusions

Volume of platelets
- 10 mL/kg (should raise platelet count by >50 × 10^9/L). Babies with suspected NAIT will require higher dose 20 mL/kg

ADMINISTRATION OF PLATELETS

Never administer platelets through an arterial line or UVC

- Use platelets as soon as they arrive on ward (ensure IV access before requesting platelets from blood bank)
- Keep platelets at room temperature
- To minimise loss, draw contents of pack into 50 mL syringe through a special platelet or fresh blood transfusion set with a 170–200 micrometre filter and infuse, using a narrow bore extension set linked to IV line, primed with sodium chloride 0.9%
- Transfuse platelets over 30–60 min, mixing syringe from time to time to avoid platelets settling down
- There is no need for routine use of diuretic after platelet transfusion
- Check platelet count 1 hr after transfusion
NEONATAL ALLO-IMMUNE THROMBOCYTOPENIA (NAIT)

- This is analogous to Rhesus haemolytic disease and is caused by transplacental passage of maternal alloantibodies directed against fetal platelet antigens, inherited from father but absent in mother.
- Majority caused by antibodies against platelet antigens, HPA-1a (80%) and HPA-5b (10–15%).
- NAIT can affect first pregnancy and has a 10% risk of severe intracranial haemorrhage; 20% of survivors exhibit significant neurodevelopmental sequelae.

Recognition

- For HPA-1a antigen-negative women, complete a neonatal alert form.
- Petechiae, purpura, excessive bleeding and severe thrombocytopenia in an otherwise healthy term newborn infant indicate NAIT until proved otherwise.
- NAIT can also present with:
  - fetal intracranial haemorrhage or unexplained hydrocephalus.
  - postnatal intracranial haemorrhage in term infant.

If NAIT suspected, involve consultant neonatologist immediately.

Assessment

- Check baby’s platelet count daily until >100 × 10^9/L.
- Check mother’s platelet count (may already be in maternal notes).
- Obtain blood from mother, baby and father for platelet typing and antibodies. Liaise with haematology department about appropriate samples.
- Arrange cranial ultrasound scan.

Treatment

- In 30% of cases, maternal antibody may not be found and can be detected later.
- Treat babies with suspected NAIT empirically with antigen-negative platelets.
- Transfuse baby with suspected NAIT with accredited HPA-1 antigen-negative platelets if:
  - bleeding or
  - platelet count <30 × 10^9/L
- National Blood Transfusion Service has a pool of suitable donors, and platelets are available at short notice from blood bank.
  - if accredited HPA-1a negative platelets not available, administer random donor platelets.

Inform blood bank and consultant haematologist as soon as NAIT suspected. Do not delay transfusion for investigations.

- If thrombocytopenia severe (<50 × 10^9/L), or haemorrhage persists despite transfusion of antigen-negative platelets, administer intravenous human immunoglobulin (IVIg) 400 mg/kg/day for 3 consecutive days.
- Aim to keep platelet count >30 × 10^9/L for first week of life, or as long as active bleeding continues.
- Report newly diagnosed babies with NAIT to fetal medicine consultants for counselling for future pregnancies.

NEONATAL AUTO-IMMUNE THROMBOCYTOPENIA

Clinical features

- Caused by transplacental passage of autoantibodies in women with ITP or SLE, and affecting about 10% of babies born to such women.
- Severity generally related to severity of maternal disease.
- Risk of intracranial haemorrhage in baby <1%.
Management

- Report all women with thrombocytopenia and those splenectomised through Neonatal Alert System, and instigate plan of management
- Send cord blood for platelet count
- Check baby’s platelet count 24 hr later, irrespective of cord blood result
- If baby thrombocytopenic, check platelet count daily for first 3–4 days or until >100 × 10^9/L
- If platelet count <30 × 10^9/L, whether bleeding or not, treat with IVIg (dose as in NAIT)
- Discharge baby when platelet count >100 × 10^9/L
- For babies requiring IVIg, recheck platelet count 2 weeks later. A few may require another course of IVIg at this time because of persistence of maternal antibodies